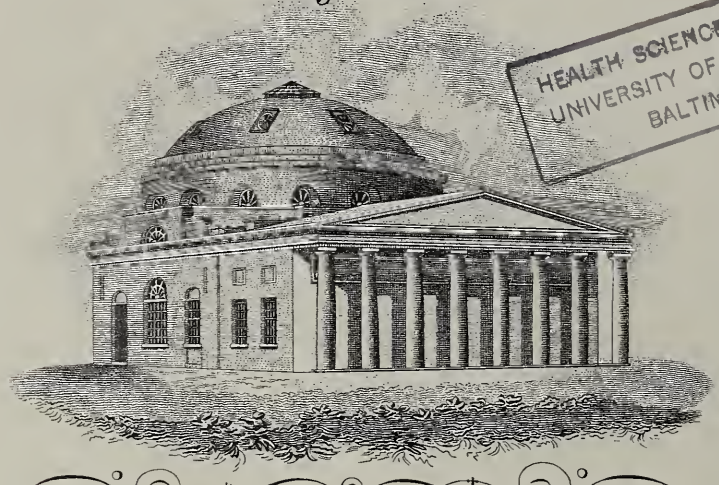
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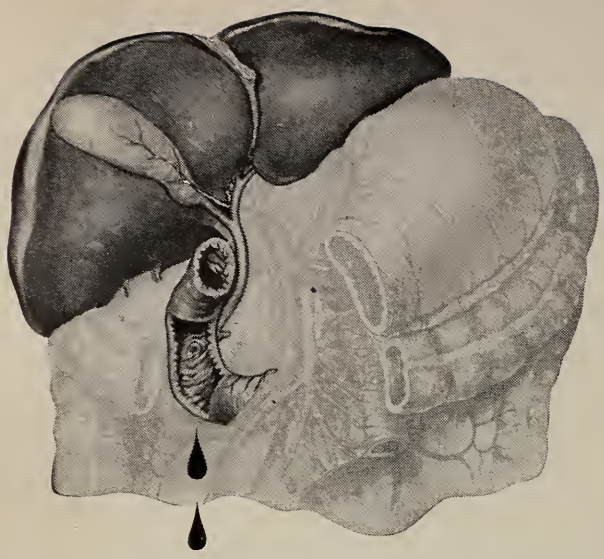
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*Albrecht, F. K.: Modern Management in Clinical Medicine, Baltimore, The Williams and Wilkins Co., 1946, p. 170.

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U. S. ON WAY TO SOLVING HEALTH PROBLEMS, JOURNAL EDITORIAL SAYS

America is "on the way toward the development of a plan for the production and distribution of medical services suitable to the American democracy," states an editorial in the current issue of *The Journal of the American Medical Association.*

Speaking of the National Health Assembly which met in Washington, D. C., May 1-4, the editorial says in full:

"The National Health Assembly which heralded the beginning of May in Washington, D. C., established what is apparently a new record for such conferences. Definite efforts were made to ascertain points of view, to attach proper weight to each of them and, on the basis of the evidence submitted. to propose recommendations which might be considered objectives or goals in advancing health during the next ten years.

"Previous conferences have been suspected of having propaganda in behalf of certain proposals leading to legislation as their prime motivation. If that was the original intent of the National Health Assembly of 1948, and it seemed to be such—when the proposed assembly, its financial supporters and executive committee were announced a few months ago, the subsequent developments and the final action taken have resolved the doubts and anxieties.

"For this, credit should be assigned perhaps to Mr. Ewing and his associates, notably Dr. Howard Kline, who evolved for the original executive committee of 24 members with only one physician, a final committee aggregating 39 with official representation for the American Hospital Association, the American Dental Association, the Conference of State and Provincial Health Officers, the American Medical Association and similar bodies.

"On this executive committee will fall the final responsibility for evaluating the recommendations that come from the different panels or sections and for issuing a final statement to clarify objectives in health for the people of the United States.

"Between 700 and 800 interested members of almost every agency in the United States concerned even remotely with health registered in this assembly. At least half of them were enrolled in sections devoted to such topics as medical personnel, local health units, research, nutrition, maternal and child health, chronic diseases and age, medical care and other significant classifications.

"These sections held four or more meetings in which opportunity to speak was given to any of those who wished to be heard on the subject of their own experiences or their criticisms of the opinions and experiences of others.

"As might be anticipated, panaceas, short-cuts, regimentations and revolutions were offered as solutions of the problems in the advancement and development of medical services.

"The bizarre and weird recommendations of radical proponents for remaking our system of medical care fell by the wayside. The recommendations of the steering committees in the individual panels seemed likely to yield technics for steady and continuous progress in meeting our medical needs.

"In subsequent issues of *The Journal* the reports

(Continued on Page 14)

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U. S. ON WAY TO SOLVING HEALTH PROBLEMS, JOURNAL EDITORIAL SAYS

(Continued from Page 12)

of each of the panels will be made available. The recommendations may be given consideration by the appropriate councils, committees and bureaus of the American Medical Association and by the House of Delegates, which will speak for the American Medical Association as to the policies considered acceptable.

"Fortunately in this assembly, as contrasted with the National Health Conference of 1938, the American Medical Association was represented by competent experts in each of the fields concerned. Several members of the Council on Medical Service participated in the panel on medical care.

"Chairmen in several sections, notably maternal and child health, research, local health units, medical care, physical medicine, hospital facilities and mental health, were distinguished Fellows of the American Medical Association.

"Members in adequate numbers served on the panels devoted to rural health, community organization, public health, hospitals, personnel and environmental sanitation. The association had available, moreover, its public relations and publicity staff and additional members on the executive committee.

"The President of the American Medical Association and the Editor of *The Journal* spoke before meetings of the entire assembly. The president-elect, members of the Board of Trustees and of the various councils addressed the individual sections.

(Continued on Page 16)



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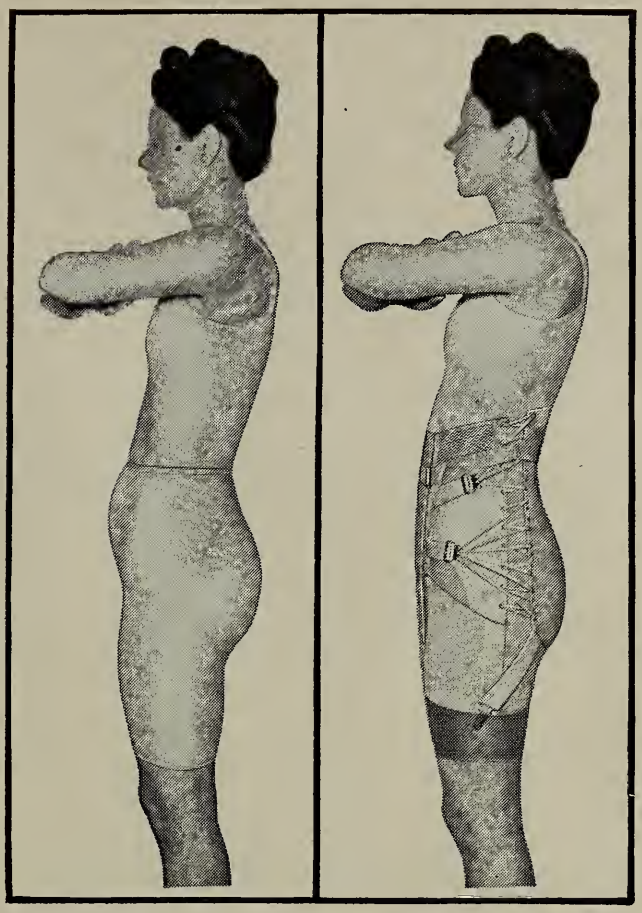
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U. S. ON WAY TO SOLVING HEALTH PROBLEMS, JOURNAL EDITORIAL SAYS

(Continued from Page 14)

"Clearly apparent from the first note sounded by Mr. Oscar Ewing in his opening address was recognition of the fundamental importance of a high quality of medical education for the solution of every medical problem.

"Second in emphasis was the necessity for consumer and professional cooperation in the development of adequate medical care at costs within the range of the mass of the people.

"Third was a perception of the necessity for continued experimentation in the development of technics of providing and distributing medical care suitable to the needs of a diversified population under varying economic conditions.

"Fourth was emphasis on the special problems of the Negro physician and the Negro patient. Such corollary questions as the availability of animals for experimentation, of funds for conducting the medical schools and research institutions on a high plane, hospitalization and health centers, technics of transportation of the sick for rural areas, cooperatives for health, group practice, medical insurance on a service or free-for-service basis and elimination of the profit motive in prepayment plans developed extended discussion and indicated the need of more study by experts.

(Continued on Page 22)

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References: 1. Gold, Harry: In Conferences on Therapy, N. Y. State J. of Med., Mar. 1, 1947. 2. Goodman, L. and Gilman, A.: The Pharmacological Basis of Therapeutics, The Macmillan Co., New York, 1941. 3. Osol, A. and Farrar, G. E.: Dispensatory of U.S.A., J. B. Lippincott Co., Philadelphia, 24th ed., 1947. 4. Sollmann, T.: A Manual of Pharmacology, W. B. Saunders Co., Philadelphia, 7th ed., 1948. 5. Loc. cit., p. 750.

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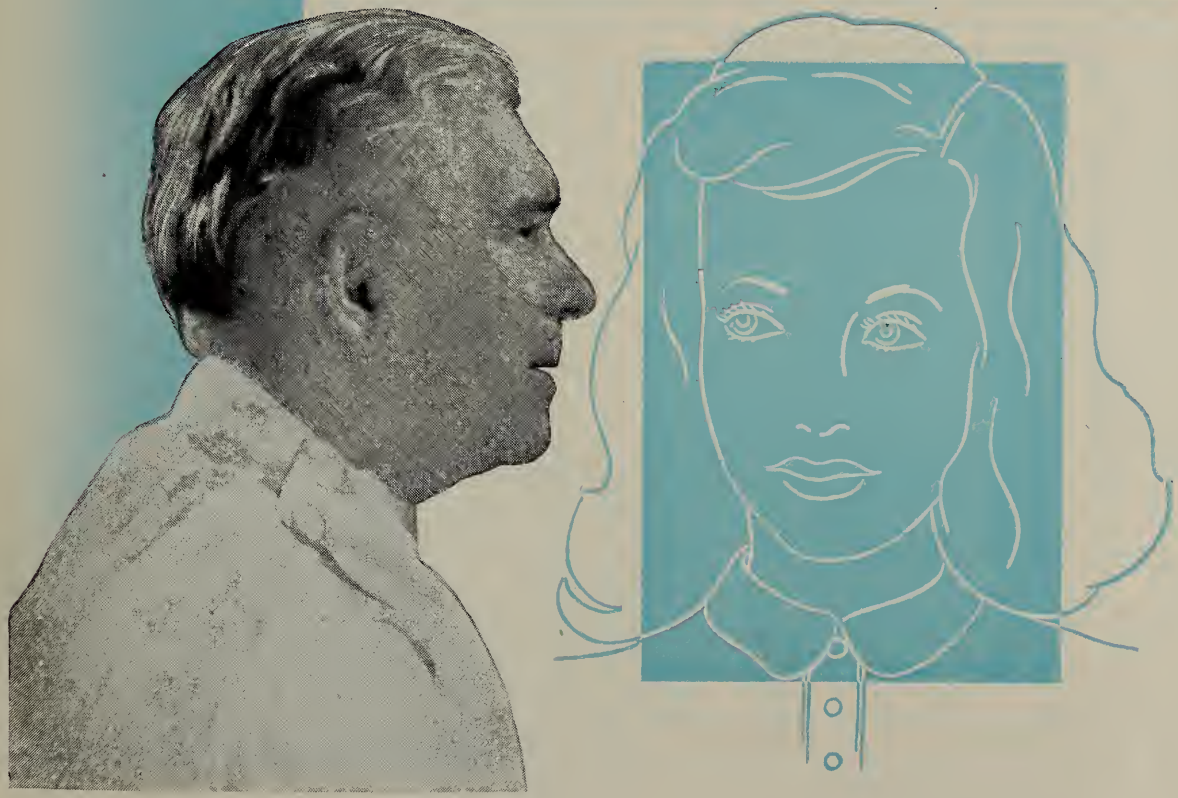
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ENGLISH DIET INCREASES BIRTH RATE, JOURNAL REPORT SAYS

Severe food restrictions and rationing have played an important part in improving the health of England and increasing her birth rate, two Boston investigators say in an article appearing in a recent issue of *The Journal of the American Medical Association.*

The report, which is on nutritional needs during pregnancy, was written by Bertha S. Burke, M.A., and Harold C. Stuart, M.D., both from the Department of Maternal and Child Health, School of Public Health, Harvard University, Boston.

In their article they state that "under the severe restrictions imposed by war, England appears to have profited considerably with respect to health as a result of her need to utilize all her available food as efficiently as possible," adding that "although the diet has been extremely monotonous, the average nutritional quality of the English diet has been improved."

Speaking of the effect of diet on the English birth rate, the authors add:

"Previous to the war, the diet of the pregnant woman in the lower income brackets in England was poorer than that of the average adult, but during the war special attention was focused on her diet. For the first time in the history of England, special food was made available to all pregnant women in the form of additional milk, eggs, supplementary vitamins and other extra rations when possible."

Studies show, the article says, that there was a sharp drop in the stillbirth rate in England and Wales after the rationing program was instituted, adding that the decrease was greatest in the poorest economic districts, such as Wales, where it amounted to 35 per cent.

The investigators point out that "these conditions occurred at a time when all conditions of life other than nutrition had deteriorated."

The report also reveals the results of studies in other countries, many of which have contributed to the knowledge of the effect of nutrition on pregnancy.

In Holland, for example, it was found that during the "hunger months" of the war and right after, about 50 per cent of the women suffered from amenorrhea and were presumably infertile. However, the article states, "this condition disappeared promptly with the return of food."

The study in Holland also disclosed that the birth weights of infants born at full term decreased suddenly during the hunger months and rose almost as abruptly as the country emerged from the severe starvation period.

In the United States, results of studies also show definite relationship of diet to pregnancy and birth.

In a group of 216 cases, studied at the Boston Lying-In Hospital, all of the stillborn infants, all except one of the infants who died in the neonatal period, all except one of the premature infants, most of the infants with congenital defects, and all of the infants considered to be "functionally immature" were born to women in the poorest diet group.

In contrast, the study showed that 94 per cent of the infants born to mothers on good or excellent diets during pregnancy were in good or excellent physical condition at birth.

(Continued on Page 24)

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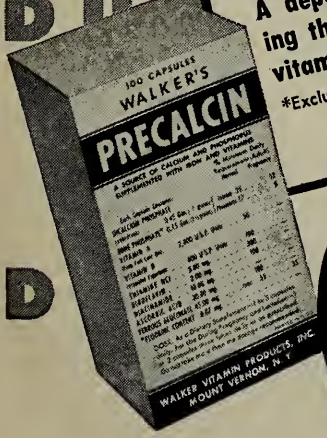
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U. S. ON WAY TO SOLVING HEALTH PROBLEMS, JOURNAL EDITORIAL SAYS

(Continued from Page 16)

"President Harry S. Truman, the only speaker at the opening banquet, indicated again his deep concern over the health problems of the nation and his continued conviction that a compulsory sickness insurance system is an acceptable solution. By far the majority of representatives of the medical profession present could not concede on this point. The voices raised in support of this contention were the same old, and now somewhat weary, voices of the Physicians' Forum, Committee on the Nation's Health, the economists of the national headquarters of the A. F. of L. and the C. I. O. When the tumult and shouting died, the record seemed to indicate that the Blue Cross Hospitalization Plans, the nonprofit voluntary prepayment plans, the cooperatives, the group health associations, the private agencies and other forms of organization for the delivery of medical services had enrolled millions and millions of people.

"While there were still knotty problems not yet unraveled and areas of insufficiency not yet supplied, the nation seemed to be on the way toward the development of a plan for the production and distribution of medical services suitable to the American democracy."

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1. Frant, S., and Abrahamson, H.: *Brennemann's Practice of Pediatrics*, *1*:28:22, 1945.
2. Blattner, R. J.: *J. Pediatrics*, *32*:220, February, 1948.

CREMOSUXIDINE

ENGLISH DIET INCREASES BIRTH RATE, JOURNAL REPORT SAYS

(Continued from Page 20)

Commenting on this and other studies, the authors say:

"With such strong evidence that good diet during pregnancy lessens the likelihood of complications and contributes to a safer labor and delivery, there would seem to be ample reason for intensive efforts on the part of obstetricians and general practitioners to improve the diets of all pregnant women coming to them for prenatal care.

"The added evidence that women who have excellent or good diets during pregnancy are much more likely to have well-developed, healthy infants, and much less likely to have stillborn or prematurely born infants . . . increases the incentive to improve maternal dietaries."

To insure optimum nutrition during pregnancy, the authors recommend a daily diet consisting of: one quart of milk; at least four ounces of lean meat, including liver once a week; two servings of fruit, plus two oranges or orange juice; at least two cooked or raw vegetables, plus a potato in its skin; at least four slices of whole grain or enriched bread, two tablespoons of butter or fortified margarine; some form of vitamin D to supply 400 to 800 international units, and enough additional foods to supply the desired weight gain.

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HYGEIA ARTICLE WARNS OF DANGEROUS WAR TROPHIES

Deadly weapons of World War II are still killing and maiming people every day in the United States, a Treasury Department investigator warns in an article appearing in the current issue of *Hygeia*, the health magazine of the American Medical Association.

The author of the article, Robert S. Krause, Detroit, says that many of the land mines, hand grenades, unexploded shells and firearms which were carried home by American soldiers as souvenirs of the war are responsible for these unnecessary and untimely deaths.

Pointing out that American soldiers, sailors and marines have always been avid souvenir hunters, Krause states that they outdid themselves in World War II, bringing home hundreds of thousands of dangerous war weapons. Of these, he says, the majority were pistols or revolvers, although there were many machine guns, submachine guns, machine pistols, carbines, mortar shells, artillery shells, land mines, hand grenades and small aerial bombs.

Without realizing it, many of the possessors of battlefield souvenirs may be violating the National Firearms Act of 1934, which requires any person owning a firearm as defined by the law to register it with the Bureau of Internal Revenue.

The law also requires that any person wishing to acquire certain types of firearms must submit an application containing his photograph, fingerprints

(Continued on Page 30)

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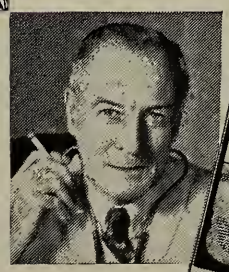
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HYGEIA ARTICLE WARNS OF DANGEROUS WAR TROPHIES

(Continued from Page 28)

and other data, and to keep with the weapon a copy of the application bearing the $200 tax stamp.

The author notes that in order to combat the high death and accident toll resulting from accidents with dangerous war trophies, several agencies, both private and governmental, have inaugurated a nation-wide safety campaign.

The program urges owners of pistols, revolvers, ordinary rifles and shotguns to have them examined by experts to see if they are safe to fire. Owners are cautioned to keep firearms away from children and thoughtless adults and are warned of the dangers of having activated explosive trophies, such as grenades. mines and bombs around the house.

The author points out that the National War Safety Trophies Committee, which was formed by the National Rifle Association, the Treasury Department, the Army and the Navy, offers to pick up dangerous weapons, have them unloaded or deactivated by experts and return them to their owners.

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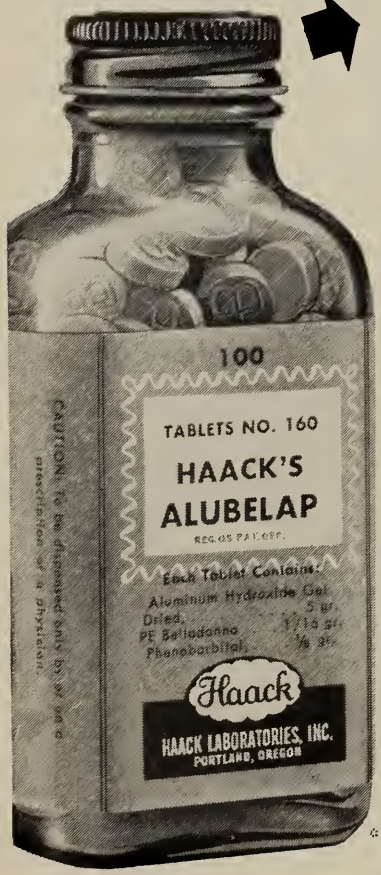
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Experimental Portacaval Anastomosis

RICHARD E. GARDNER, M.D., FRANK H. LEEDS, M.D., and
NORMAN E. FREEMAN, M.D., *San Francisco*

PORTAL hypertension, with its severe sequellae, has stimulated the ingenuity of surgeons for many years. The experiments of Nikolai V. Eck in 1877 established the foundation for the many portacaval shunting procedures that have been attempted. Direct portacaval suture anastomosis was done in France and Germany during the period from 1910 to 1912, but with poor results. Renal shutdown was the most frequent cause of death, and this was thought to be due to blockage of the inferior vena cava for too long a period. In other shunting procedures attempts were made to utilize small branches of the mesenteric veins and smaller venous channels such as the ovarian and spermatic veins. These suture anastomoses were not successful because the small vessels used did not allow sufficient flow of blood, thrombosis occurred and supportive measures that are available at the present time were lacking.

Many other procedures have been done in the hope of eliminating the hazards that result from portal hypertension. Direct cauterization of the varices, omentopexy, and attempted ligation of the small branches of the coronary vein have not met with notable success. Resection of the upper end of the stomach and lower portion of the esophagus for esophageal varices has been done with more successful results.[7] Splenectomy in cases of Banti's syndrome has resulted in occasional cures, but only when the obstruction of the splenic vein has been distal to the entrance of the coronary vein. The success in splenectomy is so variable that Blakemore[1] has urged surgeons to spare the spleen in those cases where the obstruction is proximal to the coronary vein, so that, if necessary, the patient may have the benefit of a splenorenal anastomosis.

The trying and tedious aspects of a portacaval anastomosis, as described by Whipple,[9] have been the stimulus for our experiments. We felt that if some of the technical difficulties could be overcome the operation would be considerably less hazardous. Adequate exposure appeared to be an important part of this procedure. One of us had used a transverse incision in a retroperitoneal approach to the abdominal aorta[4] which provided excellent exposure, and we felt a modification of a transverse approach would be desirable in a portacaval anastomosis.

Blakemore and Lord[2] have stated: "There is full agreement that the ideal technique in blood vessel anastomosis embraces intima-to-intima coaptation without the interposition of a foreign body in contact with the flowing blood. It is conceded that suture anastomosis, when done with meticulous care, may closely approximate the above ideal." It has recently been shown experimentally by Johns[5] that suture anastomosis results in fewer failures than the non-suture technique. Blakemore and Lord felt that suture anastomosis was impractical for portacaval shunts because of difficulties of exposure and because complete occlusion of the vena cava for the length of time required for suture technique might cause serious kidney damage. It has since been stressed by Welch[8] and Blalock[3] that complete occlusion of the inferior vena cava is not necessary. The experiments here reported present a lateral approach to the portal vein and inferior vena cava and the use of a special clamp which permits occlusion of only a portion of the latter vein during the suture anastomosis.

LABORATORY EXPERIMENTS

The present experiments were concerned with anastomosis of the end of the portal vein to the side of the inferior vena cava. Operations were carried out on 15 mongrel dogs weighing between 5 and 22 kilograms. Intravenous nembutal supplemented by ether was used for anesthesia. All dogs were intubated for the use of positive pressure anesthesia during the time that the chest was open. In the first six operations a right transverse subcostal incision was used which extended from the edge of the rectus muscle to the lumbodorsal muscle group and passed

From the Laboratories of Experimental Surgery, Division of Surgery, University of California Medical School, San Francisco 22, California. This work was supported in part by a grant from the Life Insurance Medical Research Fund.

immediately inferior to the 13th rib. The 13th rib was resected and the 12th was severed at the transverse process. This approach resulted in better exposure than the usual longitudinal incision, but the hilus of the liver was still beneath the costal margin.

A thoracoabdominal incision was found to be more satisfactory and was used in the remaining dogs of this series. A right transverse incision was made along the 10th interspace through the costal cartilages anteriorly and extending to the lumbodorsal muscle group posteriorly. The pleura and peritoneum were opened and the diaphragm was incised in the direction of its fibers, lateral and posterior to the attachment of the liver. The hepatorenal ligament was cut and the kidney was pushed down. This approach provided excellent exposure of the inferior vena cava as well as the portal vein. The anterolateral surface of the inferior vena cava was dissected free from the entrance of the renal vein to the point where it passed beneath the liver. Dissection of the portal vein from the superior mesenteric to its bifurcation at the hilus of the liver was then accomplished.

A clamp (Figure 1) fashioned from a kidney pedicle clamp was used to occlude a longitudinal section of the inferior vena cava. A rubber-shod clamp was placed on the mesenteric vein proximal to the entrance of the splenic vein and the blood flow through the latter was controlled by a bulldog clamp. The two terminal branches of the portal vein were then ligated and the portal vein was divided (Figure 2). A longitudinal incision was made in the anterolateral portion of the vena cava, within the jaws of the clamp, to match the diameter of the portal vein. Both vessels were flushed out with saline and five zero Deknatel on a curved atraumatic needle was used for the anastomosis (Figure 3).

The following suture technique was found to be satisfactory. An everting mattress suture was placed at the hepatic end, and a new suture was placed along the posterior layer as an over-and-over continuous stitch. A second everting mattress suture was then placed at the caudal end of the anastomosis, the continuous suture was snugged up, and each of its ends was tied to an end of the mattress sutures. A continuous suture was then used for the anterior layer of the anastomosis and was tied in the same manner (Figure 3).

The clamps were removed in the following order: First the clamp on the inferior vena cava was removed, next the bulldog clamp on the splenic vein, and then the rubber-shod clamp on the mesenteric vein. After removal of the clamps, occasional slight bleeding occurred along the suture line, but this ceased spontaneously. The time required for completion of the anastomoses ranged from 12 to 40 minutes. No complications were attributed to the time taken in doing the anastomoses. Anticoagulants were not used in any of these experiments.

Dogs were sacrificed at postoperative intervals of one day to four months. Postmortem studies on all the animals of this series revealed only one case in which thrombosis had occurred. In this animal there



Figure 1.—Modified kidney pedicle clamp used to occlude a longitudinal section of the inferior vena cava.

was some angulation of the portal vein. The anastomoses in the remaining cases were patent with smooth intimal surfaces. The presence of suture material within the lumen along the line of anastomosis did not appear to be harmful. Satisfactory healing, demonstrated by microscopic sections, was present in all cases. No evidence of portal hypertension was found at autopsy, and in no animal could death be attributed to the operative procedure. Table 1 presents a summary of our experimental results.

In view of the difference in the human anatomy, it was felt that anatomical dissection should be carried out to determine the exposure to be obtained by the thoracoabdominal approach. Dissections were done on two cadavers and it was found that adequate exposure could be obtained by making the incision along the ninth interspace. The diaphragm was incised transversely and excellent exposure of the in-

Table 1

Dog No.	Date of Operation	Type of Procedure	Condition of Suture Line
1	December 16, 1946	Transverse Subcostal	Satisfactory
2	December 27, 1946	Transverse Subcostal	Satisfactory
3	May 26, 1947	Transverse Subcostal	Thrombosed
4	May 28, 1947	Transverse Subcostal	Satisfactory
5	June 9, 1947	Transverse Subcostal	Satisfactory
6	June 11, 1947	Transverse Subcostal	Satisfactory
7	June 11, 1947	Thoracoabdominal	Satisfactory
8	July 11, 1947	Thoracoabdominal	Satisfactory
9	July 21, 1947	Thoracoabdominal	Satisfactory
10	July 23, 1947	Thoracoabdominal	Satisfactory
11	July 24, 1947	Thoracoabdominal	Satisfactory
12	July 28, 1947	Thoracoabdominal	Satisfactory
13	July 29, 1947	Thoracoabdominal	Satisfactory
14	July 30, 1947	Thoracoabdominal	Satisfactory
15	October 2, 1947	Thoracoabdominal	Satisfactory

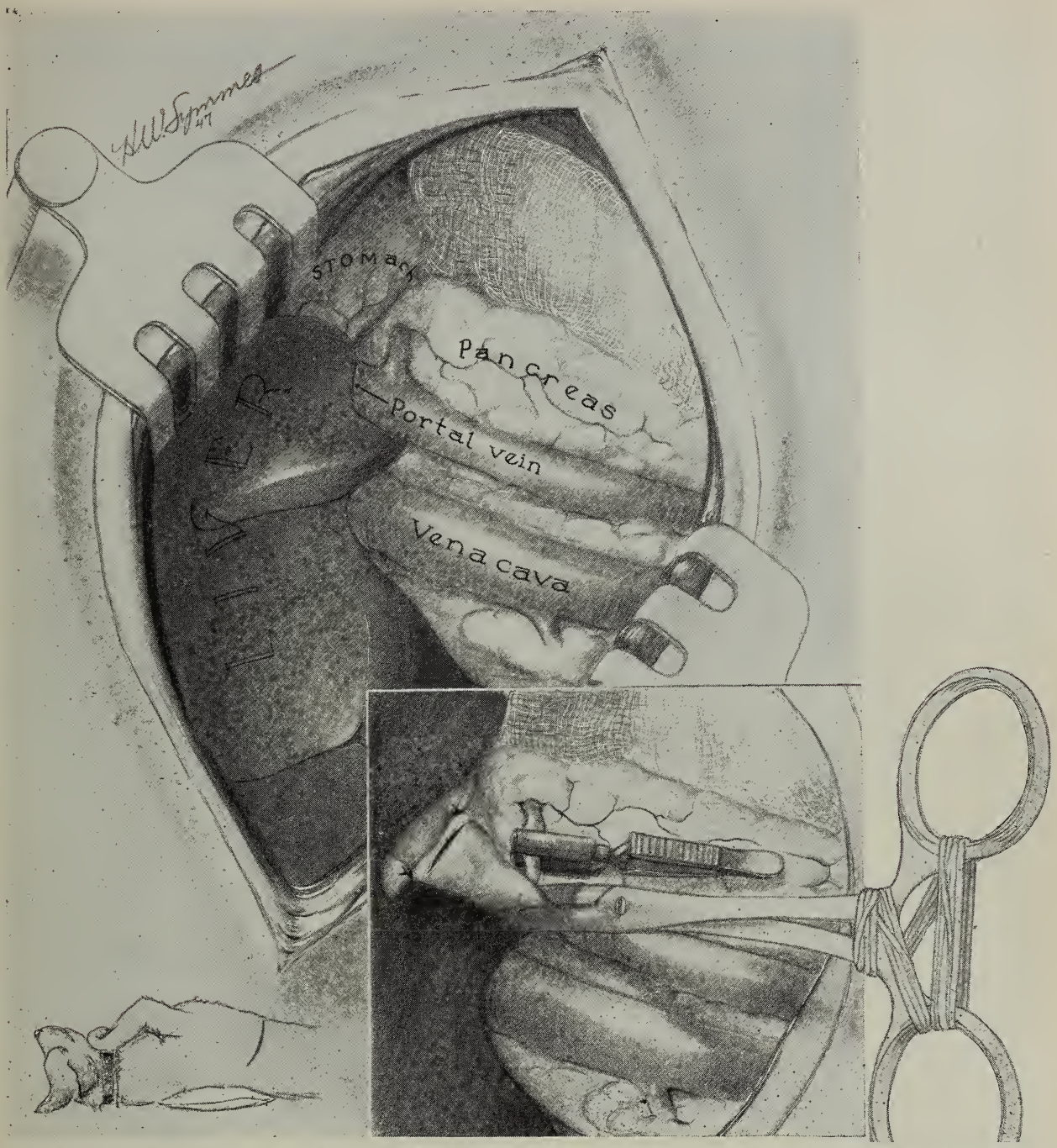


Figure 2.—Exposure in the dog of the hilus of the liver through a right transverse incision made along the tenth interspace; an inset shows portal vein ligated at its bifurcation and occluding clamps on mesenteric and splenic veins.

ferior vena cava as well as accessibility of the portal vein was obtained (Figure 4).

This procedure has been used on one patient with portal cirrhosis. A right thoracoabdominal incision was used and a direct portacaval suture anastomosis was done. This patient expired on the fifth postoperative day from hepatorenal failure. At autopsy the anastomosis was found to be patent (Figure 5).

An exploration was done in another patient through a right thoracoabdominal incision and the portal vein was found to be replaced by many small veins, a few of which were thrombosed. This was judged to be a cavernomatous transformation of the portal vein. It is now proposed to attempt a splenorenal vein anastomosis through an abdominal approach.

DISCUSSION

The clinical indications for this operation have been well discussed by Blakemore[1] and Whipple[9,10] and need be only briefly summarized. The patients are selected on the basis of liver function, the degree of disability, and the type of portal hypertension. Hypertension of the portal system is classified as to whether the obstruction is intrahepatic or extrahepatic, the former being due to cirrhosis, and the latter consisting of splenic thrombosis, cavernomatous transformation of the portal vein and various tumorous obstructions. In extrahepatic portal ob-

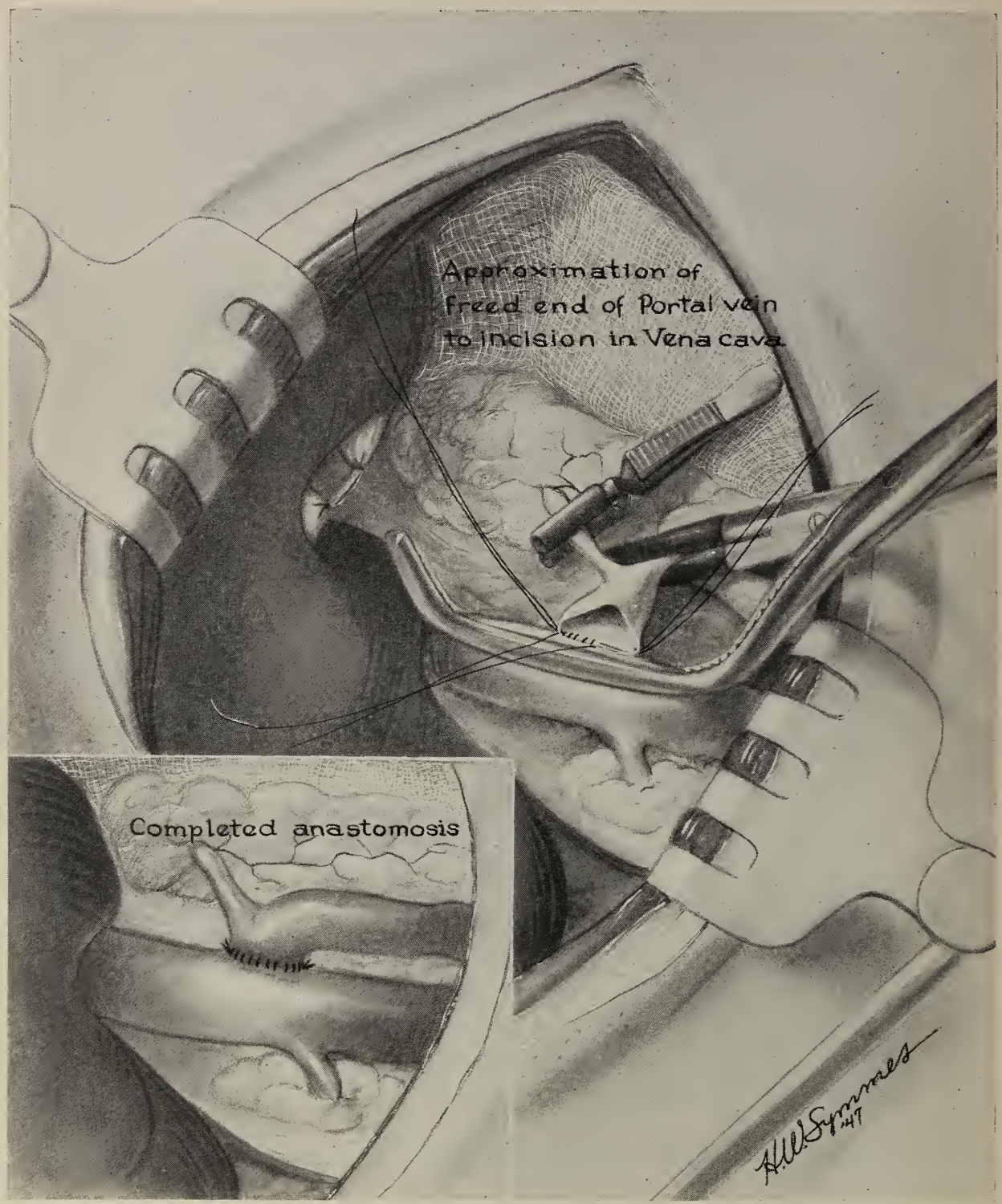


Figure 3.—Technique of end-to-side anastomosis of portal vein to inferior vena cava.

struction a splenorenal anastomosis is the procedure of choice, while in the intrahepatic obstructions a direct portacaval anastomosis would be in order.

There are cases in which the differential diagnosis of extrahepatic and intrahepatic portal obstruction is difficult, and occasionally a definite diagnosis can be made only at the time of operation. Because of this difficulty, Blakemore and Lord[2] and Blalock[3] have stressed the importance of taking manometric readings of the portal, mesenteric, and splenic veins at the time of operation in order to establish the point of obstruction. The use of liver biopsies in clinically doubtful cases may be of considerable help. This technique is a relatively innocuous procedure and has been quite successful when adequately carried out (Volwiler and Jones[11]).

In those cases with extrahepatic obstruction in which the portal vein cannot be used for anastomosis, a right thoracoabdominal approach cannot be used. A left thoracoabdominal approach, especially in

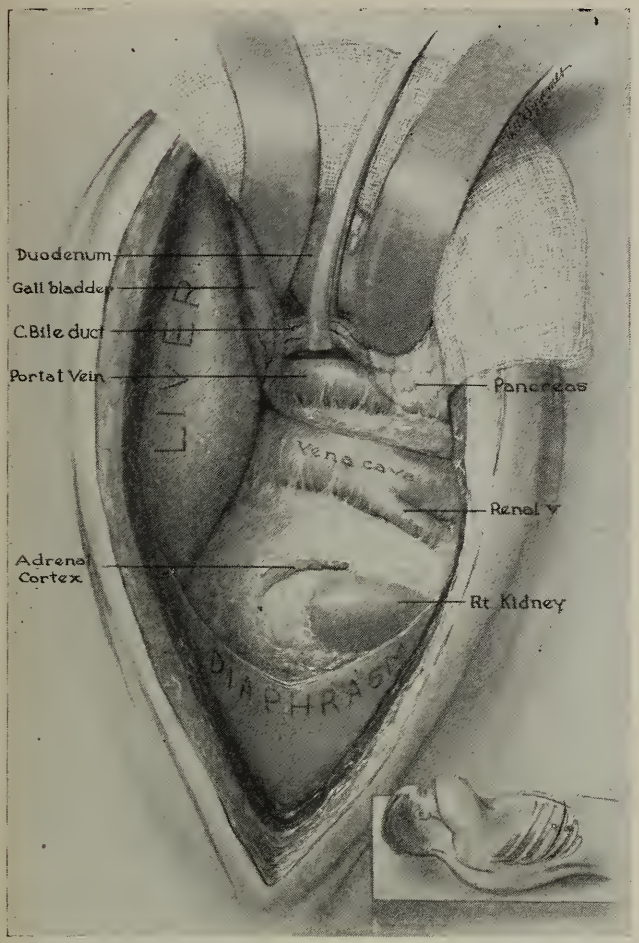


Figure 4.—Exposure of the portal vein and inferior vena cava obtained in the human through an incision along the ninth interspace.

cases where the spleen has previously been removed, has been suggested by Blakemore and Lord[2] for vein graft anastomosis of the coronary and renal veins. This approach was used by Linton, Jones and Volwiler[6] for combined splenectomy and splenorenal vein anastomosis in five cases. In cases where the diagnosis as to the type of portal hypertension cannot be established by clinical and laboratory means, it is probably advisable to proceed surgically with the plan of doing a splenorenal anastomosis. This shunting procedure should be of considerable benefit to patients with either type of portal hypertension.

SUMMARY

An attempt has been made to simplify the technical procedure of portacaval anastomosis and thereby eliminate some of its hazards. Two objections to the use of a direct suture anastomosis have been overcome. Adequate exposure has been obtained and the inferior vena cava has been occluded only partially. Suture anastomosis resulted in thrombosis in only one of fifteen animals.

The right thoracoabdominal approach described provided excellent exposure of the inferior vena cava and portal vein, and greatly facilitated the performance of the anastomosis. The use of a left thoracoabdominal approach for splenorenal anastomosis in clinically doubtful cases is suggested.

The operation in two dogs of this series was performed by Spencer T. Chester, M.D.

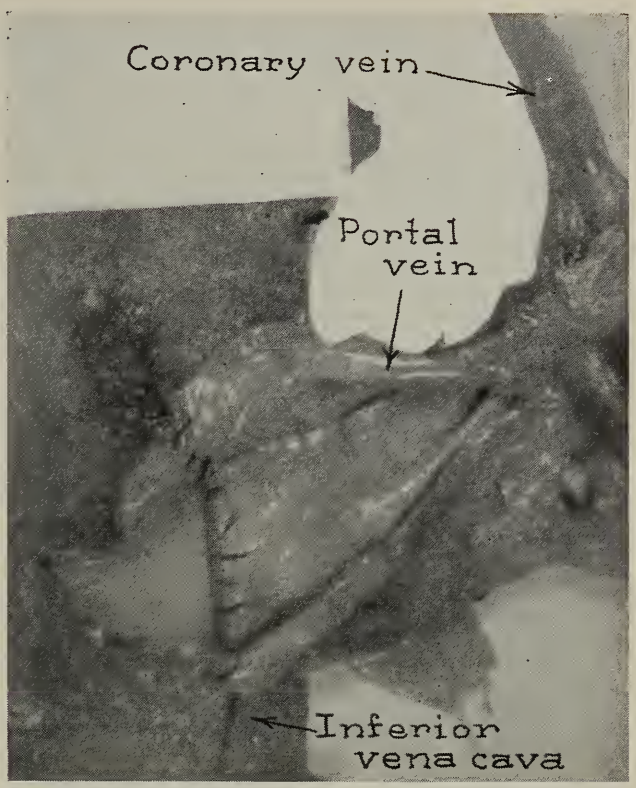


Figure 5.—Photograph of specimen obtained at necropsy five days after portacaval anastomosis.*

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* The authors wish to express their thanks to Dr. Robert O. Holmes of the Department of Pathology, University of California Hospital, for the photograph of this specimen.

Streptomycin Therapy of Tuberculosis

Seymour M. Farber, M.D., and Henry R. Eagle, M.D., *San Francisco*

SINCE the first report of the inhibitory action of streptomycin against *Mycobacterium tuberculosis* in January, 1944, interest in the clinical use of this antimicrobial agent in tuberculosis has become increasingly widespread. In a disease as prevalent as tuberculosis there is inevitably a great demand for any therapeutic agent which might possibly be of benefit. In some forms of tuberculosis the response to streptomycin therapy has been dramatic, and in others the response has been superior to that elicited by previous types of treatment. Yet in many forms of tuberculosis results have not been encouraging. Clinical experience is still too limited to allow determination of the final role of streptomycin in the therapy of tuberculosis; this must await the outcome of extensive cooperative investigations now being carried out in various parts of the world.

During the interim period of evaluation, efficient utilization of the drug depends on application of the pharmacologic and therapeutic principles thus far determined. It is the purpose of this review to summarize some pertinent aspects of the pharmacology of streptomycin and to review the current medical literature on the treatment of tuberculosis with this drug.

Streptomycin was originally discovered in January, 1944, by Schatz, Bugie and Waksman[30] and was demonstrated to inhibit the growth of tubercle bacilli in vitro.[30,31] It was then shown to have an inhibitory influence on tuberculous infection in guinea pigs by Feldman, Hinshaw and Mann[14,15] and in mice by Youmans and McCarter.[36,37] The first cases in which tuberculosis in human beings was treated with streptomycin were reported by Hinshaw and Feldman in September, 1945,[19] and by November, 1946, they had treated 100 patients.[20] Numerous reports of treatment of patients have appeared in the literature during the past year, and in November, 1947, a combined report by the Veterans Administration, Army and Navy summarized experience in 543 cases.[8]

PHARMACOLOGY

Absorption.—Parenteral injection is the usual method of administration of streptomycin, the intramuscular route being the most common. Fifteen minutes after a single intravenous injection of 600 mg. the concentration in the blood is from 30 to 35 micrograms per cubic centimeter.[41] The concentration decreases over a period of six hours to about 5 micrograms per cubic centimeter. With a single intramuscular injection of the same amount the maximal concentration in the blood is not as high as with a single intravenous injection, but the concentration is maintained at slightly higher levels over the six-hour period. Continuous intravenous infusion of 3 gm. per day produces concentrations in the blood varying between 20 and 60 micrograms per cubic centimeter. The same total daily dose (3 gm.) given in eight divided intramuscular injections at three-hour intervals produces similar concentrations of between 30 and 60 micrograms per cubic centimeter of blood. Intramuscular administration of 1 gm. daily produces concentrations in the blood varying between 10 and 20 micrograms per cubic centimeter.

Oral administration of 1 gm. daily does not produce significant concentrations in the blood. This is due not primarily to destruction of the drug by digestive enzymes, but rather to poor absorption. Animal experiments[29] have shown that adequate concentrations in the blood can be obtained if a sufficient quantity of the drug is administered by mouth. This quantity is about 30 times the parenteral dose.

When streptomycin is administered intrathecally there is good retention of the drug within the cerebrospinal fluid. Administration of from 15 to 20 mg. results in concentrations of from 13 to 25 micrograms per cubic centimeter of cerebrospinal fluid 24 hours later.[6]

Administration of streptomycin by nebulization in daily doses of 500 mg. does not result in significant concentration in the blood.[18]

Distribution.—When patients with no meningeal infection are given from 1 to 3 gm. of streptomycin daily with resultant concentrations of from 13 to 27 micrograms per cubic centimeter of blood, the concentration in the spinal fluid is from 1 to 5 micrograms per cubic centimeter, thus demonstrating that streptomycin is poorly absorbed into the cerebrospinal fluid in the presence of the normal blood-brain barrier.[41] However, when patients with meningeal infection and, hence, with a change in the blood-brain barrier, are given the same dose, higher concentrations in the cerebrospinal fluid are obtained.[1,41]

The amount of streptomycin in pleural fluid varies from patient to patient.[1,6] The concentration obtained is probably dependent upon the presence and type of inflammation of the pleura. Higher concentrations might be expected in pleural effusion secondary to constrictive pericarditis than in chronic empyema in which the pleura is thick and fibrotic.

Appreciable concentrations are obtained in peritoneal fluid in cases of peritonitis and of ascites.[6]

Streptomycin diffuses into the intra-ocular fluids.[41]

The distribution of streptomycin in the tissues and organs of the body has not been fully investigated. Data obtained from two postmortem examinations showed that most of the detectable drug was in the blood serum, kidney and bile in the gallbladder.[1] Small amounts were present in the lungs and heart muscle. Negligible amounts were found in the brain and liver. Low concentrations in the liver and spleen have also been demonstrated in mice.[27]

Streptomycin is transmitted through the placenta into the fetal blood.[18,35,41] Therefore, the same (or

From the University of California Medical Service, San Francisco Hospital, and the San Francisco Department of Public Health.

greater?) potentialities for toxicity are present in the fetus as in the mother.

Excretion.—The major excretory route of streptomycin is through the kidneys, and approximately two-thirds of the administered drug may be recovered in the urine within 24 hours.[41] The rate of excretion varies with urinary output, and the excretion is apparently accomplished by glomerular filtration.[1] A small amount (2 to 5 per cent) is excreted in the bile.[18,41]

About 2 per cent of a dose administered parenterally can be recovered from the feces.[41] This may represent biliary rather than bowel excretion. After oral administration most of the drug can be recovered from the feces.

Secretions from the tracheobronchial tree contain appreciable concentrations of streptomycin after parenteral administration of the drug.[32]

Toxicity.—Histamine reaction: The earlier preparations of streptomycin contained a histamine-like substance which produced flushing, headache and fall in blood pressure. Commercially available streptomycin is now so prepared that this reaction does not occur.

Local irritation: Intramuscular injection of streptomycin may produce soreness and induration at the site of injection. The irritation is caused mainly by impurities rather than by the antibacterial agent, and as more highly purified streptomycin is appearing on the market, this reaction is being encountered less frequently.[23] The discomfort can usually be controlled by applications of heat or cold or by adding a 1 per cent solution of procaine hydrochloride to the streptomycin solution.

Although most patients tolerate the daily instillation of from 50 to 100 mg. of streptomycin intrathecally, the drug produces definite irritation of the meninges. The severity of this irritation is roughly proportional to the total dose and is greater when less highly purified streptomycin is used.[23] Even when the dose is from 10 to 20 mg., pleocytosis commonly occurs.[6] Rarely, there are symptoms of this meningeal irritation. Some individuals complain of pain over the sacrum lasting for from 12 to 24 hours after the intrathecal injection.[23] In prolonged courses this reaction usually disappears after one or two weeks. As much as 275 mg. administered intrathecally once daily for several weeks has been tolerated by some patients, but many patients have reactions to this high dose.[13] The reaction occurs in less than one hour and consists of headache, vomiting and nystagmus. The patient becomes somnolent and respirations slow, and there may be urinary retention. The reaction gradually subsides in the course of 48 hours. Administration of a 1 per cent solution into the pleural and peritoneal cavities has been well tolerated.[23]

Hypersensitivity: Various manifestations of hypersensitivity may occur during streptomycin therapy.[13,23] Occasionally the patient's temperature will rise to from 102° to 104° F., five to seven days after the beginning of a course of the drug. In approximately 5 per cent of patients dermatitis occurs. The dermatitis resembles the common forms of drug rash and may be associated with eosinophilia and constitutional symptoms of varying severity. Rarely, exfoliative dermatitis may appear. In a large proportion of patients eosinophilia will develop either with or without dermatitis during prolonged courses of treatment with the drug. These allergic reactions seldom give cause for permanently discontinuing therapy. However, since the relationship of drug hypersensitivity to diffuse vascular disease is not clearly understood, such reactions may possibly carry long-term serious potentialities.

Renal toxicity: Often cylindruria and occasionally albuminuria occur unassociated with hematuria or nitrogen retention. These conditions are apparently of no significant consequence and may be minimized or eliminated by alkalization of the urine.[13,23]

In a small proportion of patients definite reduction in renal function develops, as evidenced by a decrease in the result of the urea clearance test and rise in concentration of blood urea nitrogen. This reduction in function may be an advanced form of the same process which produces the benign cylindruria, but its exact relationship to the cylindruria is not known.[23] In almost all instances it has occurred in patients who had renal disease prior to streptomycin therapy. It has not been established whether alkalization of the urine will prevent the development of this condition, but for the present such a precaution seems warranted.

Neurotoxicity: In almost all patients receiving streptomycin in prolonged courses and in large doses, damage to vestibular function will develop.[8] If administration of the drug is continued, this reaction leads to complete and presumably irreversible loss of vestibular function in the majority of cases. The onset occurs at the end of about the fourth week of therapy with doses of from 1 to 2 gm. daily and at about the end of the third week with doses of 3 gm. daily.[23] Often the first sign is a headache which subsides in 24 hours. The patient then notes the onset of dizziness. This is not true vertigo, as the rotary component is lacking. The sensation is accentuated by movement, and the patient has a sense of "overshooting the mark," although the past-pointing phenomenon cannot be demonstrated. Sometimes nausea and, rarely, vomiting occur. The acute symptoms last for approximately seven to ten days, after which the patient begins to learn to compensate for the lost vestibular function. The degree and rapidity of development of compensation vary from patient to patient, and older persons have a poorer ability to compensate. Patients may experience difficulty in walking in the dark after compensation has taken place, but accommodation is usually good in from 60 to 90 days. While the loss of vestibular function is not of serious import to the average patient in comparison with the disease for which streptomycin is being administered, it is conceivable that it would have a profound effect on patients who are blind or who have disease of the posterior columns or cerebellum.

Under certain conditions, use of streptomycin will

cause nerve deafness.[23] However, this deafness is not a common occurrence. It has been reported to occur (1) during intrathecal therapy for meningitis, (2) during prolonged intramuscular therapy with excessive doses (4 to 10 gm. per day) and (3) in the presence of renal insufficiency with retention of excessive concentrations of streptomycin in the blood. It has been reported that the first sign of impending cochlear damage is a low-pitched continuous roaring tinnitus.[5] Discontinuance of use of the drug when the tinnitus begins would probably prevent significant auditory loss. In a few instances, when there has been definite but incomplete auditory loss, discontinuance of use of the drug has revealed that this loss is partially reversible. Continuance of streptomycin therapy may result in complete deafness.

The site of the lesion causing these neurologic abnormalities is not known with certainty at present, but there is limited evidence that liquefaction necrosis of the vestibular and cochlear nuclei is involved.[23]

Blood dyscrasias: Eight instances of blood dyscrasias occurring in association with streptomycin therapy have been reported.[8] Five of these consisted of mild leukopenia with neutropenia and the other three consisted of agranulocytosis. Thrombocytopenia may occur rarely.[9]

Dosage and route of administration.—Intramuscular: The results of investigation of the optimal dose of streptomycin are just beginning to appear in the medical literature. Until recently a policy of giving as large doses as possible without invoking symptoms of major toxicity has been followed by many clinicians. Presumably the upper limit of reasonable tolerance is about 3 gm. daily, and 2 to 3 gm. daily has been a commonly utilized dose. However, the incidence of vestibular nerve damage from use of these large doses has been very high (96 per cent of 543 patients receiving 2 gm. daily for 120 days),[8] and investigations have been undertaken to evaluate lower dose schedules. Although reports of this work have not as yet been published, an editorial resume in *The Journal of the American Medical Association*[12] announced encouraging preliminary results. Therapeutic effects of the use of 1 gm. daily were similar to those produced by use of 2 gm. and the incidence of vestibular toxicity was reduced to about 20 per cent. The frequency of appearance of predominantly resistant organisms was not altered.

The frequency of injection is also undergoing change as a result of recent investigations. Formerly, the daily dose had been divided into four to eight portions and administered at three to six-hour intervals in an effort to maintain a reasonably constant concentration in the blood. Feldman, Hinshaw and Karlson[16] demonstrated that division of the daily dose into two portions and administration at 12-hour intervals was as effective in inhibiting tuberculous infection in animals as administration at shorter intervals. Preliminary studies[12] in man with doses of 0.5 gm. every 12 hours apparently affirmed the therapeutic effectiveness and showed that toxicity is not increased. There is experimental evidence[11] that tuberculous infection in guinea pigs may be maximally inhibited by one injection of streptomycin every five days and partially inhibited by one injection every ten days. It thus appears likely that the maintenance of a constant concentrating of streptomycin in the blood will not prove to be necessary and that the drug will be administered less frequently than it is now.

The duration of effective intramuscular therapy is limited by the frequent occurrence of bacterial resistance. Cultures in nearly all cases may be expected to exhibit predominantly resistant organisms after 120 days of streptomycin therapy. Although patients are commonly treated for from 90 to 120 days, investigation of shorter schedules is now under way.[24,26]

Inhalation: When streptomycin is administered by inhalation of a nebulized solution, the commonly used daily dose is 500 mg., dissolved in 10 cc. of physiologic saline solution and given in 5 to 10 portions.

Intrathecal: The optimal intrathecal dose in tuberculous meningitis has not been determined. A daily injection of 100 mg. has been used frequently, but it more recently has been suggested that 50 mg. is a preferable dose.[12] Intrathecal injections are usually administered every one or two days. Specific data concerning the optimal duration of intrathecal therapy in tuberculous meningitis have not been reported. Persistent return of the concentration of sugar in the spinal fluid to a normal figure might or might not be a logical guide.

It should be emphasized that the therapeutic results cited in a subsequent section of this paper have been obtained with intramuscular and intrathecal doses larger than the currently advocated amounts. In summary, in the treatment of tuberculosis the present recommendation[12] is that 0.5 gm. of streptomycin be given intramuscularly every 12 hours for 120 days, except in cases of miliary and meningitic tuberculosis, when use of 2.0 gm. or more is advised. In meningitis the intrathecal injection of 50 mg. every one or two days is also recommended.

Action.—Almost all strains of tubercle bacilli, isolated in cases of tuberculosis in which the patients have never received streptomycin therapy, have been predominantly sensitive to the antimicrobial effect of streptomycin.[25,38] The bacteriostatic concentration in vitro was found to be 1.56 micrograms or less per cubic centimeter in 90 per cent of a series of 131 strains, and the majority of the organisms were sensitive in a concentration of 1 microgram or less per cubic centimeter.[38] The bactericidal concentration has been shown to be in excess of 50 micrograms per cubic centimeter.[39] Thus it can be seen that the concentration obtained in the blood of most patients is well in excess of the bacteriostatic concentration but is not bactericidal.

Bovine strains of tubercle bacilli are comparable to human strains in their susceptibility to streptomycin in vitro[38] and in vivo.[17]

Although cultures made prior to streptomycin therapy show predominant sensitivity to streptomycin, cultures made after treatment very frequently show predominant resistance to the antimicrobial

action of the drug. Cultures of tubercle bacilli have been shown to become resistant to streptomycin both in vitro[25,34] and in vivo.[38,40] This is one of the major limiting factors of its use in the treatment of tuberculosis. In one series, resistance was observed as early as the 35th day of therapy and occurred in 19 of 20 patients after from 90 to 120 days.[8] In another series it developed in 39 of 62 patients after from 60 to 120 days.[8] Whether the isolation of resistant organisms indicates that further streptomycin therapy will be ineffective in a particular case has not been determined without doubt, but available evidence strongly favors this view.[24,26] The resistance which develops is apparently of long duration, if not permanent, and is retained after numerous subcultures and passage through guinea pigs.[22] A study by Pyle[28] indicated that "strains" of tubercle bacilli isolated from patients before streptomycin therapy may contain small numbers of resistant organisms, although the "strains" are predominantly sensitive to streptomycin. This suggests that streptomycin therapy, by inhibiting the sensitive members of the strain, allows the more resistant members to flourish and eventually to become predominant. It seems likely that other mechanisms also are involved in the development of bacterial resistance to streptomycin.

CLINICAL USE

Since streptomycin does not have a uniform effect in the several types of tuberculous infection, the reported results of therapy will be discussed under various disease types.

Primary phase tuberculosis.—No extensive reports of treatment of the primary phase are available. In view of the favorable prognosis presented by a proper conservative regimen of therapy, streptomycin apparently has no place in the treatment of this type of infection at present.

Reinfection phase pulmonary tuberculosis.—Minimal pulmonary tuberculosis: The prognosis in cases of minimal reinfection with use of adequate bed rest and collapse therapy, when indicated, is favorable in at least 90 per cent of cases. In view of the hazards of toxicity and of the development of bacterial resistance, streptomycin is not recommended as an initial form of treatment.

Moderately and far advanced pulmonary tuberculosis: In this condition cavities may be thick walled, the structure and physiology of the lung may be altered by fibrosis, and vascularity in many of the diseased areas may be diminished. It might be expected that a bacteriostatic agent would have limited value in significantly affecting a disease in which these conditions are present.

In a carefully studied series of 157 cases[8] it was demonstrated that streptomycin therapy had little effect on old fibrous or caseous lesions but was associated with improvement in the majority of exudative lesions. Although exudative lesions frequently exhibited striking regression, resolution of these lesions was rarely complete, and relapse after completion of treatment was frequent.

Hinshaw and his associates[21] did not recommend employing streptomycin in the treatment of chronic fibrocaseous pulmonary tuberculosis unless conspicuous evidence of recent exudative disease is found. They also emphasized that streptomycin has little to offer if the rapidly progressing exudative lesions are merely part of a terminal phase of overwhelming infection.

Muschenheim and his colleagues,[26] in a study of 43 patients, also found that exudative pulmonary tuberculosis responded more favorably to streptomycin therapy than fibrocavernous disease. Although the incidence of sustained satisfactory remission was not high, less complete improvement sometimes allowed surgical collapse in cases not suitable for such measures before streptomycin treatment.

Tuberculous empyema: After intramuscular administration, usually concentrations of streptomycin in empyema fluid are reasonably high. However, the results of parenteral treatment or of instillation of streptomycin into the pleural cavity are not encouraging. Hinshaw, Feldman and Pfuetze[20] reported that improvement occurred in one of seven cases and suggested both the acidity of the empyema fluid and the granulomatous nature of the disease as being unfavorable factors.

Bronchogenic dissemination.—Recent pulmonary spreads: Favorable results of treatment of these lesions were reported by Hinshaw, Pyle and Feldman,[21] by Canada,[7] and by Muschenheim and his colleagues.[26] As the pathologic process is usually exudative, streptomycin may prove of value when resolution does not take place under conservative therapy.

Tuberculous tracheobronchitis: Brewer and Bogen[3] reported a series of 44 cases of ulceration and granulation of the trachea and bronchi. They divided these into several groups and employed streptomycin by aerosol and in various doses intramuscularly. Aerosol therapy (500 mg. daily) alone and intramuscular injection of 0.5 gm. and 1.0 gm. respectively, daily were partially effective, while intramuscular injection (2.0 gm.) alone and intramuscular injection in combination with aerosol therapy were each effective in 13 cases.

Tuberculous laryngitis: Black and Bogen,[2] and Hinshaw, Pyle and Feldman[21] reported favorable results in the treatment of this condition. In 34 cases[2] in which varying doses and varying routes of administration were used, lesions healed in 13, improved in 17 and were unimproved or worse in four. These results were definitely superior to those achieved in similar cases with former methods of therapy.

Hematogenous dissemination.—Acute generalized hematogenous dissemination (miliary tuberculosis): Arrest of miliary tuberculosis in several isolated instances has been reported, and there is no doubt of the therapeutic effect of streptomycin on this type of infection. However, study of large series of cases revealed that the disease still carries a very significant mortality rate.[8,24] The major causes of failure of streptomycin therapy in this instance are the develop-

ment of bacterial resistance to streptomycin and the occurrence of a complicating tuberculous meningitis during therapy. Until prolonged follow-up studies have been completed, the incidence of recurrence and the ultimate mortality rate in cases of streptomycin-treated miliary tuberculosis cannot be determined. However, present evidence suggests that the mortality rate is significantly reduced by use of the drug.

Tuberculous meningitis: A number of apparent arrests of this condition due to streptomycin have been reported. Arrest of this type of tuberculosis presents a striking demonstration of the influence of this antibiotic agent on tuberculous infection. However, the effect of such treatment on the ultimate mortality rate of the disease has not yet been determined. That the effect will not be as favorable as that in miliary tuberculosis without meningeal involvement is generally conceded; and that use of streptomycin will alter an eventually fatal outcome has been doubted by some investigators.[8] In a series of 91 cases of tuberculous meningitis in which the drug was used,[8] 58 of the patients died, and at the time of the report in only 18 of the remaining 33 cases had treatment been completed and the infection apparently arrested. The percentage of these 18 cases in which relapse may be expected to occur is unknown. The intrathecal, as well as the intramuscular, route of administration has been strongly advocated in this disease. Although in cases of meningitis significant concentration of the drug in the spinal fluid is obtained by intramuscular administration, intrathecal administration produces a concentration which may be bactericidal rather than only bacteriostatic. It is desirable to decrease meningeal infection as rapidly as possible, for prolonged inflammation will produce lesions mechanically incompatible with life, even though bacteriostasis is eventually obtained.

Osseous tuberculosis: Satisfactory response to streptomycin therapy of this condition was noted by Hinshaw, Feldman and Pfuetze,[20] but others have reported less satisfactory results.[8] We have observed two patients with single osseous lesions which regressed strikingly during streptomycin therapy. It is anticipated that results with this type of infection will be variable.

Tuberculous lymphadenitis: The results of treatment of enlarged tuberculous nodes are variable.

Genito-urinary tuberculosis: Cook, Greene and Hinshaw[10] and Hinshaw, Feldman and Pfuetze[20] reported the results of treatment in 15 cases of renal tuberculosis with tuberculous cystitis. They noted marked symptomatic improvement in 50 per cent of cases and a reduction in the degree of bacilluria in the majority. However, return of symptoms and bacilluria was a frequent occurrence, and they felt that use of streptomycin was palliative rather than curative. It has been emphasized that streptomycin therapy is not a substitute for nephrectomy in cases of unilateral renal tuberculosis.

Tuberculous enteritis.—There is, as yet, no basis for defining the place of streptomycin in the treatment of enteric tuberculosis. Final evaluation of treatment will be difficult, since antemortem diagnosis of this condition may be uncertain. Sweany noted marked symptomatic improvement in a few cases.[33]

Tuberculous sinus tracts.—Sinuses originating in bone or lymph node and fistulae originating in the gastro-intestinal tract are strikingly affected by streptomycin. Brock[4] reported closure of 59 of 60 sinuses (12 patients) and emphasized the importance of establishing surgical drainage whenever indicated. It is frequently necessary to carry out debridement of necrotic bone and similar procedures to obtain maximal benefit.

Miscellaneous tuberculous infections.—Few cases of streptomycin therapy in tuberculous pericarditis, peritonitis, dermatitis, ocular lesions and other tuberculous complications have been reported. After use of streptomycin, improvement has been noted in some of these extrapulmonary lesions.[8,20]

Adjunct to surgical treatment of tuberculous lesions.—Since streptomycin therapy has shown promise in cases of recent spread of pulmonary tuberculosis, there is a rationale for preoperative and postoperative administration of the drug in cases of tuberculosis in which thoracoplasty, lobectomy or other such procedures are performed. It might be hoped to reduce the incidence of contralateral spread and tuberculous empyema after operation. Evaluation of this adjunctive therapy will take place as an increasing number of patients are studied.

SUMMARY

On the basis of these reports there appear to be indications for streptomycin therapy in the following conditions: laryngeal and endobronchial tuberculosis, miliary tuberculosis, tuberculous meningitis, osseous tuberculosis, tuberculous lymphadenitis, sinuses and fistulae, and exudative tuberculous pulmonary lesions not responsive to conservative therapy. In genito-urinary tuberculosis and tuberculous enteritis, streptomycin may have a place in treatment as a palliative medication.

It is desirable for the present time to limit the use of streptomycin to these types of tuberculosis for the following reasons: First, streptomycin is a definitely toxic drug. When the disease process is severe, the prognosis grave, and use of streptomycin indicated, the toxicity hazard is not comparatively great, but when the disease process can be controlled by other measures or when streptomycin has shown little promise in similar cases, the toxicity hazard cannot be taken lightly. Secondly, after a prolonged course of treatment with streptomycin, strains of tubercle bacilli frequently appear which are resistant to streptomycin. This resistance is prolonged and a return of sensitivity has not been reported. Therefore, after one course of streptomycin therapy the drug may become and remain totally ineffective and hence may be useless at a later date when the indication for its use is more urgent.

It should be emphasized that streptomycin is merely an adjunct to the treatment of tuberculosis. In the concentrations obtained in the blood, the drug is only bacteriostatic. The actual killing of tubercle bacilli and healing of lesions must be accomplished

by the immune mechanisms of the body, and the patient should be given all the supportive measures of modern tuberculosis therapy. Bed rest, careful dietary supervision, skilled nursing care, collapse procedures as indicated, symptomatic medication, all are necessary to obtain maximal benefit from streptomycin therapy.

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The Physician's Point of View on Regional Organization of Hospitals

JOHN W. CLINE, M.D., *San Francisco*

IT was with reluctance that I accepted the invitation to speak to you today concerning the attitude of the medical profession toward the planning of regional organization of hospital services. As far as I am aware approval of a definite plan for this purpose has not been made by the American Medical Association or any state medical association with one possible exception. Approval may have been granted to local plans by local societies but if so I am not cognizant of it.

The matter has not been widely discussed in state associations or in the American Medical Association. My opinions must therefore be based upon a wide acquaintanceship with physicians in all parts of the country and a knowledge of their reactions. Long contact with local, state, and national organizations furnishes a basis of estimating the opinion of these bodies.

It seems likely that my remarks will not be pleasing to some of you. From an analysis of the information at my disposal concerning regional organization it appears that there are in reality three phases to such plans. These involve the functions limited to hospitals themselves, staff functions, and an intermediate area where one impinges upon the other.

The medical profession has a right to expect that hospitals exercise the functions peculiar to them in such a manner that the hospital will be efficiently and properly operated. Only in this way can the physician be assured of a satisfactory place in which to care for his patients who require hospitalization. The methods and details concerned with the achievement of this end are outside the province of the physician.

It is recognized that the governing authority of the hospital is in most instances responsible for the appointment of the staff and the administrative personnel of the institution. After the staff has been created it must be autonomous in exercise of its functions. It must not be interfered with by either the governing body or the administration, provided it performs its duties in a way which fulfills the requirements of competency and ethics.

The intermediate area in which hospital and staff functions overlap is the most fruitful source of conflict and misunderstanding. Certain facilities have grown up about hospitals which involve the activities of medical personnel and the practice of medicine. Hospitals tend to look upon these as lying in the legitimate sphere of hospital activity. The medical profession tends to look upon them as an invasion of the practice of medicine. In certain instances this is clearly the case and in many states some of these activities certainly constitute a violation of the law.

In the majority of instances a reasonable adjustment between physician and hospital exists but neither party is entirely satisfied. There are practical problems which stand in the way of a satisfactory solution. Time, patience, and a mutual desire to cooperate on a reasonable basis are required of both parties if an agreeable arrangement is to be achieved. An arbitrary and uncompromising approach by either will delay or even jeopardize a proper solution.

The physician has a natural concern about all matters affecting hospitals because these necessarily involve his interests and those of his patients. He will, therefore, carefully scrutinize any program designed to change the status of hospitals. He will be on the alert for signs of an increased tendency to infringe upon his field and for any move to limit the freedom of hospitals or the profession.

As I understand the regional organization plans proposed they envision the division of hospital facilities into four groups.

1. The hub of the plan is a teaching center, consisting of a medical school and a hospital of two hundred or more beds. It would have all the facilities usually found in a medical school and a teaching hospital.
2. The intermediate or regional hospital of one hundred to two hundred beds. It would be organized with services staffed by recognized specialists but would lack research and certain teaching facilities.
3. Rural hospitals of fifty to one hundred beds equipped to care for ordinary illness.
4. Community health and medical care centers with offices for physicians and a few beds for minor illness, emergencies and "normal obstetrical cases."

It is contemplated to organize these institutions into an integrated plan which would assign certain functions and duties to each and limit them in some degree in their scopes of activity.

There is no positive statement as to who would construct the new institutions which would be necessary to such a program. There is a suggestion that finances would be derived from tax sources. The assumption is that local, state, and federal funds would be used. There are statements that existing facilities would join together under the plan on a voluntary basis. The mechanism of control of new and old facilities is not entirely clear.

It has been stated that hospitals in this country have developed on the basis of community wealth or individual benefaction rather than in response to population need. There is some truth in this statement but it does not present an accurate picture of the hospital situation in California. The present distribution of hospital beds does not reflect current needs, but one must take into account the fact that construction during the war years was almost impossible and is still expensive and difficult.

There is at present, and for many years there has been, an informal relationship between physicians, and, in some instances, between physicians and hos-

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pitals, resulting in a degree of differentiation of the types of cases treated in the facilities of local communities. There has been a tendency for doctors in rural areas, small centers of population, and even sizable cities to refer patients who were gravely ill or had complicated problems to more skillful colleagues working in better equipped institutions. This practice is not uniform and is influenced by the attitudes of the patients and the physicians. It is often determined by the competency of the local doctor and the adequacy of existing facilities.

At this point it would be well to inquire what is to be gained by a program of regional organization. It is also pertinent to ask what disadvantages it might have and how feasible it is of attainment.

The advantages claimed for it are:

1. It would "decentralize or spread out from the largest cities into the remotest hamlet all the benefits modern medicine has to offer."

2. "Small hospitals can benefit by being able to look toward the larger district hospitals for consultation service, and when necessary, can refer patients to it. Patients might even be transferred directly to the base hospital if the particular case so indicated."

3. It would bring about "the flow of professional personnel and special services from the large hospital to the small one" and "the flow of patients, specimens and records from the small to the large institutions."

4. Consultations by specialists in medical fields and advice of technical hospital experts would be furnished by the larger to the smaller hospitals.

5. The larger hospitals would train personnel to staff smaller hospitals.

6. There could be certain economies effected by pooled purchasing by groups of hospitals.

Are these real advantages? The technical fields of hospital administration are without the scope of the medical man. I shall not comment upon them, except to remark that the interchange indicated exists in some degree now and can be developed to any desirable extent without formal organization.

With reference to "decentralization" of medical care and the extension of the benefits of modern medicine to the "remotest hamlet," I would raise the question whether the reverse might not be accomplished. Would there not be a tendency toward centralization? Certainly there is central planning and there would be central direction. To make a plan such as this work would require central authority. It is apparently planned to have certain patients and patients with certain diseases cared for in certain institutions. This would necessitate promulgation of rules and regulations. The outlined plan for consultants and advisors would tend to set and enforce the pattern of conduct of smaller institutions.

Is this not an unwarranted interference with the freedom of the patient, the physician and the hospital? It suggests an effort at regimentation. It also suggests the entrance of public health departments into the practice of medicine even in the most remote rural areas.

It is claimed that the smaller hospital could look toward the larger one "for consultation service" and when necessary refer patients to it. The term "consultation service" obviously refers to medical consultation.

I would like to inquire how a hospital may know when a consultation is desirable or necessary and how a hospital may furnish a consultation. I have a firm conviction, which I believe is shared by practically all physicians, that the care of the patient, the decision as to need for consultation, the choice of the consultant and the furnishing of consultation constitute the practice of medicine and are solely and completely the function of the physician, with the consent of the patient.

By the same token, how can a hospital refer patients to another hospital? In the sense of medical care, a hospital has no patients. Persons confined to a hospital because of illness or injury are the patients of the physicians rendering care to them. It would be presumptious for an institution lacking all the qualifications for the practice of medicine to consider that it has any function in this regard. In only an occasional instance, and then only by the staff rather than the hospital, should a demand be made upon a physician to obtain consultation.

The same is true of the designed "flow of personnel" and services except as these refer to the functions peculiar to the hospital as distinct from medical fields. The hospital is likewise exceeding its prerogative if it presumes to direct the flow of patients and specimens from one institution to another. Who is responsible for the care of the patient and the examination of specimens? It is not the duty or privilege of the hospital to do these things. These are acts which can be performed only by the doctor of medicine.

It is probable that words have been loosely used in explaining this program and the intent is not that expressed. Words, however, have certain meaning. The whole field of semantics has developed about this fact. When expressions implying interference with the practice of medicine are employed it is not unnatural that the medical profession would question the intention and effect of the program.

When the foregoing statements are coupled with the fact that certain institutions engage in the practice of medicine and some hospital administrators have openly proposed that physicians be employed by hospitals to practice their profession on a salary basis, the element of suspicion in the minds of doctors is increased many fold. Let us have a frank and accurate statement of the intentions of the hospitals and program of regional organization. Unless this is done and the statement is satisfactory, not only will there be a lack of cooperation but there will be strong opposition on the part of the medical profession.

I have reviewed the plans for regional organization of hospitals for California and Michigan. Both resemble tables of operations of military organizations. To place them in full operation would require corresponding military discipline. This is found in civilian life only in the authoritarian state. Certainly none of us wishes that. It could be directly accom-

plished only by changes in the basic law of the country which would make the hospitals and the physicians subject to direction by governmental authority.

There are more insidious, indirect methods which could be employed to accomplish similar ends. The dispensation of government funds is the usual means of forcing people or organizations into the acceptance of dictation. Funds could be, and in fact are, made available only to institutions conforming to certain rules laid down by those who dispense the funds. Reasonable conformity to standards of construction and operation cannot be objected to but it could be a short step from this requirement to acquiesence in control and operation.

There is also the possibility that some units of government might build hospitals to be operated in competition with existing facilities. You may believe this remote. I hope it is, but I would call your attention to the rapid increase in veterans' hospitals, public ownership of certain hospitals not designed for mental or communicable diseases, the perversion of some of our county hospitals and the determined assault upon the means test. It is not beyond the realm of possibility, and should it occur it would sound the death knell of private hospitals and the freedom of medicine.

You, as hospital people, are in a much better position than I to know, but it is my impression that private hospitals are operated upon a more efficient and economical basis than are corresponding public institutions. In those with which I am acquainted it is true.

It is my opinion, which I believe is almost universal among physicians, that with the exception of care of indigents, persons with mental or communicable disease, and certain other classes of individuals, government has no place in the field of hospitalization.

A hazard is ever present in the use of government funds for hospital construction. As yet this has not involved control, but funds can be obtained only by compliance with rigid regulations which at times may be unreasonable. The old adage that "he who pays the piper calls the tune" is still true. The greater the utilization of tax funds from federal or other sources, the greater will be the measure of governmental control.

The bureaucrats with their expanding desire for power will not be content to sit idly by and watch uncontrolled grants-in-aid continue. They inevitably will strive to extend their control under the guise of beneficent regulations.

The politicians have not refrained from interference in hospitals for indigents and those for special classes of patients. Consider the great temptation to control the affairs of institutions designed for paying patients.

Let us now return to the planning of regional organization. The community health and medical center is supposed to be flexible in size and form. In smaller areas it is contemplated to staff it at intervals with visiting teams. It is a place in which "preventive" services are to be found along with medical care for illness. Where does one draw the line between the two? How are these services to be provided? Could this arrangement not become an opening wedge for the extension of the activities of public health departments into the practice of medicine? We are in need of a clear delineation of the proper functions of public health departments, a limit beyond which they should not and cannot go in the field of medical care.

The larger center is designed for the care of emergencies, ordinary illness, and "normal obstetrics." Is this a practical arrangement? How grave is an emergency and what preparation is necessary for its care? Is the prospective mother whose labor is interrupted or whose placenta separates prematurely to be submitted to cesarean section at the center, or to be transported a considerable distance while in a serious condition? Who is to make these decisions—the administration, some higher authority, or the physician? Would it not be wiser to plan for obstetrical care in a better-equipped facility?

The rights, powers, and duties of the board of controlling authority and the administrator of the hospital are described in some detail. Nowhere do I find the practice of medicine defined. The physician is charged with duties but enumeration of his rights and powers is omitted. Is this omission the result of intent or oversight? If the latter, does it indicate a philosophy of relegating the physician to a secondary status?

It is stated, "Ideally, it would appear that the hospital is the logical place to refer patients for all types of diagnostic procedure." I reiterate that diagnosis of disease constitutes the practice of medicine, an activity denied the hospital by law. Even if this were not true, one would be impelled to ask what basis is there for the belief that the hospital could provide a more accurate diagnosis than the practitioner of medicine and is it the intent of the hospital to displace the private physician?

"A well organized outpatient department should be an integral part of the hospital and the health service of the community" is another statement requiring scrutiny. There is no mention of a means test. The logical conclusion would be that it is recommended that the hospital foster an outpatient department to compete with the physician. This is again the practice of medicine.

Associated diagnostic clinics are advocated: "Employing the principle of group practice, they avoid duplication of equipment, save time of the attending physician, are more convenient for patients and permit more effective medical care." By and large, group practice does these things to an insignificant extent if at all. "Effective medical care" depends upon the abilities of the individual physician whether in a group or alone. I have no criticism of group practice for those who wish it. Certain physicians find it desirable for reasons which pertain to their own welfare. Others do not. It is presumption for a hospital, a state agency or other organization to tell physicians how their practices should be conducted. It is dis-

tinctly not in their province and to attempt to set up diagnostic clinics in the hospitals is again the invasion of the field of medicine unless these facilities are designed for indigents.

In the minds of the medical profession the hospital exists for the purpose of extending the scope of medical care. In fulfilling that purpose it is an independent allied service and is not and cannot be the dominating and directing force in medical care. After all, the physician sees many patients in his office or in the home for every patient he sees in the hospital.

An apparent attempt to limit the freedom of the physician is found in this statement: "The rules and regulations adopted by staffs *and governing boards* of small hospitals should be based upon facilities and indicate the limitation of medical practice within the institution." Any limitation of medical practice must be purely a staff function. One may ask what do boards of laymen know about the problem and by what right do they propose to adopt rules governing medical procedures. This idea shows a fundamental lack of understanding of medical care.

It disregards entirely the capabilities of individual staff members. I have taught medical students, interns and residents for years and have followed the careers of many as they have established practices in different communities. I know something of their abilities. I also participate in the examination of candidates for the American Board of Surgery, and in this way come in contact with men of ability who have had excellent training and who are practicing in various communities throughout the West. For some years I have served as a member of the Applicants Committee and the Credentials Committee of the American College of Surgeons for Northern California.

As a result I have examined the records of operations of men from all parts of this area. There are well trained and competent surgeons in communities too small for more than a rural hospital who are performing creditably and successfully practically all the procedures of general surgery. In some instances they possess abilities at least as great as their colleagues in nearby cities of greater size. Who is to gainsay men of this type? Certainly not a board of laymen.

Let us now consider the feasibility of this program. Without methods of force, it can be effective only to the degree the patient, the hospital and the physician wish to make it so.

The physician must determine which patient should be referred to another physician. He must also decide where and to whom the patient should be sent. The patient must make the decision as to whether he wishes his care to be rendered at home and by a local physician or elsewhere and by someone else. The freedom of the patient and the physician cannot be abridged. Neither will permit it.

The average physician is more concerned about the welfare of his patient than any other item. He knows his own limitations and the limitations of the facilities available to him. If he does not recognize these he can be dealt with on a local level but not by a statewide plan imposed from without.

Hospital cooperation is not within my scope but I doubt if many of you would be willing to bind your institutions to a plan which would circumscribe their functions and development. Certainly no one would suggest that a first-class hospital in a small community should be reduced in size or scope to meet a prearranged population pattern.

In such a program local civic pride will be encountered. Rivalry between neighboring communities is often intense. Population limitation on size, character and scope of hospitals will not generally be accepted by the citizens. This has already been demonstrated in California. Perhaps unwisely from an economic point of view some localities desire more extensive facilities than the State Department of Health believes justified.

Population growth varies and population shifts occur. Who can be sufficiently certain of the future to say with assurance that some of these communities may not be more wisely planning for their future needs than those who would prescribe arbitrary standards for them?

The medical profession is opposed to extending the regulation of the lives of individuals and their activities. The whole plan of regional organization is reminiscent of the promulgations of other planners of the recent past. The desire to decide what is good for others goes hand in hand with progressive limitation of individual freedom and progressive increase in the power of the State.

The idea impresses me as a bit grandiose in its ambition. There is no way of achieving Utopia in one easy lesson.

The value of an idea, if it has value, becomes more apparent upon free and general discussion. The medical profession, I am sure, has no objection to and would favor presentation of such a program to the people, the profession and the hospitals. It likewise would not object to the educational effort to convince these groups of the desirability of parts of the plan. But the presentation must be fair and frank and the right of the medical profession to decide all aspects of the plan dealing with medical care must be respected.

The medical profession recognizes the need for reasonable regulations, licensure and inspection of hospitals, but it would resist perversion of this function of government to bring about an integrated plan of regional organization of hospitals.

It likewise will object to and oppose direct governmental action by legislation and indirect efforts to accomplish this end by selective use of tax funds.

Evolution of ideas is superior to revolution. Compulsion is anathema to the American people and the medical profession. The main objectives of regional organization may be brought about in time if their wisdom and desirability can be demonstrated, but this can be accomplished only on a voluntary basis.

Let us proceed in this manner with due regard for all the elements of medical care involved and on a basis of mutual respect and cooperation. Only in this way can we hope to achieve constructive results of importance and permanence.

490 Post Street.

X-Ray Diagnosis and Therapy in Arthritis

M. F. Godfrey, M.D., *Glendale*

SATISFACTORY diagnosis of the arthritides is frequently difficult except by roentgenographic study of skeletal structures. The late S. Gilbert Scott of London in his monograph on the rotengenological examination of the hands in the arthritides dubbed the hand "the calling card of the arthritic patient." In his book he stated that in systemic forms of arthritis the hand is usually involved even though there may be no subjective findings locally.

Four main types of arthritic or rheumatic conditions are seen by physicians with much greater frequency than are other types. They are the following:

1. Osteo-arthritis (synonyms: Degenerative arthritis, hypertrophic arthritis). This form of arthritis affects both males and females, principally in the latter half of life, and in all climes.

In the hands the distal joints of the fingers appear nodular (Heberden's nodes), and sometimes the distal phalanx is tipped slightly to one side. The roentgenogram reveals narrowing of the cartilages of the joints involved. The involvement is usually bilateral. There may be associated similar involvement of the proximal interphalangeal joints. The articular ends of the bones become broadened and show a tendency toward proliferative bony changes at the periphery of the articular surfaces. The involved joints in the more advanced stages may also show a hill and valley grooving of the badly worn articular ends of the bones. The other joints of the hand and wrist are rarely involved. A very important feature is the normal bone density present. No osteoporosis is present in osteo-arthritis. This type of arthritis is degenerative and is the type also found associated with occupational traumata.

2. Rheumatoid (also called proliferative or atrophic) arthritis is quite a different problem, not only clinically but also roentgenographically. It is found more frequently in women of child bearing age and in emotionally unstable people. It is sometimes found in males. It is not a degenerative disease but is an acute or subacute illness which may be devastating to a few or many of the joints of the body. It is usually found in the joints of the extremities, but it may involve the spine and/or the shoulder and hip girdles.

In the hands there is destruction of the cartilages of the proximal joints of the fingers, the metacarpophalangeal joints, and the carpal regions, and there is fusiform soft tissue swelling about the proximal joints of the fingers. The distal joints of the fingers are uninvolved. It is usually bilateral and in more advanced cases there is frequently ulnar deviation of the fingers. There is a definite tendency, sometimes quite marked, toward osteoporosis. No new bone is laid down about the joints but there is usually considerable soft tissue proliferation or swelling about the involved joints, hence the term proliferative arthritis. The hands usually feel cold and clammy. When rheumatoid arthritis involves the spine, the joints of the extremities usually escape, and, conversely, when it involves the extremities, the spine usually escapes. The cause of this geographic variation is not understood.

In some cases the first evidence of disease in the back is found in the sacro-iliac joints. When this occurs the first roentgenographic evidence of disease is a loss of sharp definition of the outlines of a part of or all the articular surfaces of one or both of the sacro-iliac joints. As the condition progresses more and more of the definition of the joint is lost until finally the entire articulation takes on a blurred appearance. Later, in rheumatoid arthritis, actual bony ankylosis occurs. Clinically the patients usually have tenderness over the sacro-iliac joints. The degree of tenderness varies widely. Recurrent attacks of low back pain are usual phenomena. (Rheumatoid spondylitis will be discussed later in this paper.)

3. Gout. Only 32 per cent of persons with gouty arthritis show bone changes in the roentgenogram, even in the late stages of the disease. When signs are present on roentgenograms, there are definite punched-out appearing areas in the subchondral bone at the heads or bases of the long bones of the hands or feet. This may be so advanced as to cause destruction of the articular surfaces of one or many joints. Gouty arthritis may be either unilateral or bilateral. In 70 per cent of cases the first attack appears in the metatarso-phalangeal articulation of the great toe, and it may appear in this region and not in any other location.

Gout does not always show bilateral distribution in the roentgenograms. However, many cases of gout are not associated with roentgenographic evidence of the disease until late. Gout is much more frequent in males but may be found in either sex after adulthood. It is more frequently found after middle age. It is more destructive when found in young people. The uric acid content of the blood is elevated in about 75 per cent of cases. The disease is sometimes found in people who drink no alcoholic beverages and who live on a simple diet.

4. Non-articular or soft tissue rheumatism causes no bony changes other than occasional inflammatory roughening of the periosteum of the long bones. It is frequently associated with capsulitis and pericapsulitis, as well as inflammation of the sheaths of the tendons. There is evidence of inflammation of the fibrous tissue in the muscles, as was observed by F. F. Roynd. This is frequently fleeting in character and tends toward spontaneous remission in its earlier phases. Later it may be constant and, when chronic. is usually associated with arthritic changes in the joints. It may be as painful as any of the arthritides.

Read before a joint meeting of the Sections on General Practice, General Medicine and Urology at the 76th Annual Session of the California Medical Association in Los Angeles, April 30-May 3, 1947.

RADIATION THERAPY

Roentgen ray therapy locally over inflamed joints may be used to relieve pain. In this capacity it may be used in osteoarthritis, rheumatoid arthritis, gouty arthritis, or in cases of capsulitis, pericapsulitis, bursitis, or tendinitis. It is quite dramatic in the relief of the intense pain sometimes associated with capsular or pericapsular inflammation, usually three or four treatments sufficing to relieve the pain and reduce the immobility of the joint. In sciatic neuritis, the results of roentgen ray therapy are only partially satisfactory, particularly in acute cases.

All forms of heat treatment make the skin more sensitive to roentgen rays. Hence it is well to avoid such treatment for at least a week before and a week after roentgen radiation has been given. This includes diathermy, hot air, light, short-wave therapy, ointment dressings, plasters, hot packs, etc. Luetics, even when in a symptomless stage, tend toward a stronger skin reaction than other patients.

In advanced osteoarthritic changes in the lumbar region, considerable relief frequently follows radiation of the lumbar muscles. This has been well attested by Kahlmeter in 1929 and again in 1937, by Von Pennewitz in 1933, and Scott in 1937, and by other writers. This is probably due to improvement in the circulation of these muscles and their aponeuroses; with radiation the muscle spasm is lessened. According to Scott, Kaplan, and others, roentgen rays improve circulation as well as increase lymphocytic activity.

Radiation therapy is also of some palliative value in advanced degenerative arthritis of the hip, the so-called malum coxae senilis. The relief appears to be largely due to relief of muscle spasm. Radiation therpay does not deter the degeneration of the joint.

The author's radiation technique is briefly, as follows: For the elbow, wrist, ankle, shoulder, hip, and knee, 100 to 150 r per treatment, the dose depending upon the size of the joint, treating twice weekly and employing, over the larger joints, two ports, an anterior and posterior, until four to eight treatments have been given. A second course of four treatments may be given after a rest period of from six to twelve weeks.

Spondylitis of the rheumatoid type, according to the late S. Gilbert Scott, usually begins as arthritis of the sacro-iliac joints; he described cases in which the first roentgenographic evidence of disease was in the sacro-iliac joints. In most of his cases he was able to elicit histories of growing pains through childhood and early adulthood. Furthermore, a considerable number of his patients had been athletes; quite a number of them had been excellent swimmers.

At least 90 per cent of ankylosing spondylitis occurs in men. According to Ehrlich the average age of onset is 31 years. It is not familial.

The disease usually begins with pains or aching in the lower back; frequently the first discomfort is a "lumbago-like" painful attack which comes and goes. Each occurrence is more painful and persistent than preceding ones. The soreness then extends out into the gluteal regions and up the back. Permanent stiffness, according to Crowe, usually occurs in from one to five years after the onset of rheumatoid spondylitis. During this period the patient loses weight, becomes easily fatigued, irritable and introspective.

Goldthwait and his co-workers, in their excellent monograph on body mechanics, describe the psysiologic changes resultant from this postural change. The chest is flattened and the posterior mediastinum is practically obliterated so that the diaphragmatic movements are seriously impaired and portal circulation is thereby greatly decreased.

The inflammatory changes in the soft tissues of the back are followed by calcification in the anterior, posterior and lateral ligaments of the spine as well as of the interspinous ligaments. The so-called bamboo spine is thus produced. It is also known as the Marie-Strumpell spine. With the calcification of these structures the mobility of both the spine and thoracic cage is lost and the patient thereafter stands in a kyphotic posture with the shoulders thrust forward, the chest flat and the lumbar curve largely lost. Lung expansion is much impaired. Though the end result is painless the condition does not burn itself out until the patient is a "burned out spondylitic wreck."

As to treatment, Scott and Kahlmeter are outspoken in their favor of roentgen ray therapy. Khalmeter stated in 1932 that "there are few fields in x-ray therapy in which the results are so reliable and satisfactory as they are in arthritis." This statement has been well borne out by the experience of Freiburg and many others.

Roentgen ray therapy for spondylitis is as follows: Radiation is given along the entire spine, using a port 10 cm. wide and radiating the entire spine by segments, not more than half the spine receiving radiation at one sitting. A dose of 75 r is given to each field twice weekly for three weeks. Following a rest period of two months, four to six treatments are given as a second course. The patient should then be watched for 12 months and if the condition tends to return, a third and shorter series may be given. Not more than 1,000 r should be given any one field. The clinical response is indeed gratifying. The crippling muscle spasm and pain is overcome and mobility of the spine, so far as muscle spasm is concerned, is restored. No other method of therapy for spondylitis offers the patient this degree of early and lasting relief.

Roentgen treatment for bursitis of joints is dramatic in suddeness of relief at times. For instance, in bursitis of the shoulder, in which the pain is sometimes agonizing, much relief may be experienced 12 to 24 hours after the first treatment. Our experience coincides with that of Young in that there is a higher percentage response in acute cases than in those of longer standing. Four treatments given either daily or at two-day intervals usually relieve the spasm and pain. It is well to take a roentgenogram of the joint before therapy is undertaken, to rule out recent or old fracture and primary or metastatic bone diseases. Also, it is well to know if calcification exists in bursae

about the joint. We know, however, that calcareous deposits are frequently present without symptoms.

Our series of patients treated with wide-field body radiation is too small to warrant discussion. Scott, in his monograph, "Wide Field X-ray Treatment," reports excellent results. Our limited experience thus far has not given similar response.

330 North Central Avenue.

Acute Central (Hypopyon) Ulcers of the Cornea

PHILLIPS THYGESON, M.D., *San Jose*

CENTRAL corneal ulcers form a group of ulcers distinct etiologically and clinically from marginal corneal ulcers.[6] In contrast to the latter, which typically are secondary to acute and chronic conjunctivitis, central ulcers are primary in the cornea. The seriousness of the typical (pneumococcic) central ulcer, moreover, is in sharp contrast to the typical benignity of the typical (staphylococcic) marginal ulcer. A further point of difference is that the causal organisms of central ulcers can almost invariably be found in scrapings from the ulcer base while scrapings from marginal ulcers are often disappointing.

The following report summarizes the results of an etiologic and therapeutic study of 50 cases of central ulcer observed by the writer since 1932. They do not constitute a consecutive series since only those cases are included for which records of etiologic determinations were retained and in which therapy was personally administered or supervised.

CLINICAL CHARACTERISTICS

The central ulcers in this series varied in severity from mild, slowly progressing infections, readily amenable to therapy, to the exceptional fulminating infection which, in the matter of a day or two, progressed to destruction of the eye. As will be discussed later in detail, the different etiological types, although indistinguishable on purely clinical grounds, varied considerably in severity.

The typical central ulcer arose most often near the margin of the cornea and then progressed in a band-like process into and across the pupillary area. Hypopyon was a characteristic feature in all but three of the 50 cases and tended to develop early in the disease. Pain was severe in most cases and photophobia was prominent in all but four cases in which the ulcers occurred in insensitive corneas. Conjunctival reaction was usually mild.

Although the ulcers could be considered primary in comparison with typical marginal ulcers, they were in fact invariably secondary to corneal epithelial damage of one sort or another, the most common being that resulting from corneal foreign bodies. Other sources of epithelial damage included rupture of corneal bullae in bullous keratitis, fingernail scratches, and lacerations from branches of trees in agricultural workers. The possibility of an occupational relationship was suggested by the fact that 12 of the 35 pneumococcic ulcers were in coal miners and three of the four pyocyaneus ulcers were in railroad trainmen.

ETIOLOGY

No difficulty was encountered in determining cause in any of the 50 cases. Scrapings from the advancing borders of the ulcers invariably showed the causal bacterium in large numbers, and its final identification was always possible on culture. In sharp contrast to the findings in the series of marginal ulcers previously reported by the writer,[6] there were no cases in which either smear or culture findings were negative. All five of the bacteria found could be recognized in scrapings taken directly from the lesions. Thus an immediate presumptive identification of the infecting organism was always possible—a matter of considerable importance in view of modern antibiotic therapy and chemotherapy.

Table 1 outlines the etiologic findings for the series. In each instance identification of the organism was confirmed in culture. As was to have been expected, the pneumococcus was causal many times more frequently than the other agents. Its nearest competitor was the beta hemolytic streptococcus, with Pseudomonas aeruginosa (pyocyaneus bacillus) next in order and followed by the Diplobacillus of Petit and Klebsiella pneumoniae.

The only difficulty encountered in the identification of the bacteria in culture was in connection with

TABLE 1.—*Bacteriological Findings in 50 Cases of Central Ulcers of the Cornea*

(Organisms identified in smear and culture)	
Diplococcus pneumoniae	35
Streptococcus hemolyticus	6
Pseudomonas aeruginosa	5
Diplobacillus of Petit	3
Klebsiella pneumoniae	1
	50

From the Department of Ophthalmology, Division of Surgery, University of California School of Medicine, San Francisco.

Read before the Section on Eye, Ear, Nose and Throat at the 76th Annual Session of the California Medical Association in Los Angeles, April 30-May 3, 1947.

the one Friedlander bacillus ulcer. The familiar problem of distinguishing between Klebsiella pneumoniae and Aerobacter aerogenes necessitated the use of type-specific sera as developed by Julianelle for precipitin tests. The organism from the ulcer was found to fall into Julianelle's type A.

In Gram-stained preparations the two Gram-positive bacteria, Diplococcus pneumonia and Streptococcus hemolyticus, were easy to differentiate since the pneumococci were typical morphologically and invariably encapsulated. The three Gram-negative bacteria were also readily differentiable. Typical diplobacillary morphology distinguished the Diplobacillus of Petit while the encapsulation of the Friedlander bacillus distinguished it from the unencapsulated pyocyaneus bacillus. The capsule of the Friedlander organism, unlike the capsule of the pneumococcus, stained faintly but definitely with the Gram counterstain and was thus in no danger of being confused with the so-called "retraction spaces" sometimes seen in smears which have been heat-fixed.

THERAPY

Pneumococcic ulcers. The first 21 of the pneumococcic ulcers of this series were seen prior to 1938, before the sulfonamide drugs came into use. The only chemotherapeutic agent then available was optochin and the results obtained with it were not sufficiently striking for it to have replaced the standard method of cauterization with a thermal cautery. Optochin applied in powder form to the ulcers after curettage of the ulcer base failed to arrest progress in the three cases in which it was tried; in all three thermal cauterization was necessary later. The remaining 18 were all treated primarily by thermal cauterization of the advancing border. This method was generally effective in controlling the infection but good visual results were obtained only when the ulcer had started in the periphery and had not yet advanced into the pupillary area. Cauterization in the pupillary area inevitably resulted in a significant drop in vision. There was no loss of the globe in any of the 21 cases.

Shortly before the introduction of the sulfonamide drugs, serotherapy of pneumococcic pneumonia had come into general use as the result of studies which led to the recognition of 32 distinct serological types. The writer undertook preliminary studies which showed that typing by the "Quellung" phenomenon of specific capsular swelling was a practical procedure, but with the introduction of the sulfonamides the intention of trying serotherapy was abandoned.

Since 1938 cauterization has not been employed by the writer in any case of central ulcer. Reliance has been placed entirely upon sulfonamide and antibiotic therapy, supplemented in a few cases with foreign protein therapy. Sulfanilamide, sulfapyridine and sulfadiazine have all been used. In the first few cases they were given orally only but it was soon realized that in central ulcers topical administration of the drug was of more importance than oral administration. Sulfadiazine was employed orally and topically in eight of the twelve sulfonamide-treated cases, the topical application being in the form of sulfadiazine powder dusted into the ulcer crater after curettage and into the lower fornix every three or four hours. Atropine was of course used to dilate the pupil. In all eight cases this treatment resulted in rapid resolution of the disease with a minimum of cicatrization. Sulfanilamide was used in the first three cases before sulfapyridine and sulfadiazine, which were found to be much more effective, became available. Sulfadiazine is to be preferred to sulfapyridine because of its lesser toxicity.

Only two pneumococcic ulcers in this series were treated with penicillin but the results were eminently satisfactory.The antibiotic was employed intramuscularly in a dosage of 20,000 units every three hours, and topically in the form of instillations every half hour of a solution containing 1000 units per cc., and in the form of iontophoretic applications of the sodium salt twice daily, according to the method outlined by von Sallmann.[7] In both cases rapid resolution with a minimum of cicatrization resulted.

Streptococcic ulcers. The six beta hemolytic streptococcic ulcers were all treated with the sulfonamides, one with sulfanilamide and five with sulfadiazine. The first case of streptococcic infection in the series, which occurred in 1938 just after the introduction of sulfanilamide, was in a young woman who had received a corneal scratch in the pupillary area of the left eye. When the patient was first seen there was dense infiltration in the pupillary area which had reduced the vision in the eye to recognition of hand movements. The ulcer crater itself was about 3 mm. in width. Scrapings from the base showed numerous Gram-positive round cocci in diplococcal form and in short chains, and culture revealed pure beta hemolytic streptococci which were found to have an exalted virulence for the rabbit cornea. Treatment with sulfanilamide was started immediately, a dosage of 1 gm. being given every four hours. Improvement was manifest within 24 hours and healing within three days. The resultant scar was nebulous in character, and vision was 20/30 + one month later. The visual result in this case is believed to have been infinitely better than could have been expected if cauterization, either chemical or thermal, had been used instead of the sulfanilamide.

In the five sulfadiazine-treated cases oral therapy was supplemented by topical applications of the drug in the form of powder or 5 per cent ointment. Response was rapid in all five cases and the resultant scars were small.

Pyocyaneus bacillus ulcers. Three of the five pyocyaneus ulcers were seen prior to the introduction of the sulfonamide drugs. All three were in railroad employees who developed the ulcers after having had corneal foreign bodies removed in the same office. Pyocyaneus bacilli growing in fluorescein used for staining the corneas were believed to have been the source of all three infections. In each case the ulcer progressed to loss of the globe in spite of chemical cauterization combined with topical applications of various antiseptics.

Unlike the preceding three patients, who were re-

ferred for treatment only after the ulcers were well advanced, the remaining two were seen when the disease was early in development. Both were treated with sulfadiazine orally and topically (by iontophoresis and powder) and in both cases the response was good. The resultant scars were minimal.

Diplobacillary ulcers. Two of the patients with Diplobacillus of Petit ulcers were seen in consultation and were the second and third of a group of three reported by Chamberlain, Elliot, and Givner.[2] As reported by these authors, the treatment in the first of the two cases consisted in the instillation of 1 per cent zinc sulfate solution three times daily, and the instillation of 0.5 per cent zinc sulfate ointment nightly. Under this treatment the ulcer slowly improved, but as the eye was blind and painful from long-standing glaucoma, enucleation was performed. The second ulcer followed multiple corneal foreign bodies and, without treatment, progressed slowly over a period of five days to cover the lower half of the cornea. Local therapy consisted in a linear keratotomy, topical application of zinc sulfate solution and ointment, and one application of the thermophore at 158°F. to the base of the ulcer for one minute. Systemic therapy consisted in sulfanilamide 1.3 gm. four times daily for ten days, followed by sulfapyridine 1 gm. four times daily for one week. Two injections of foreign protein were given, one of 5,000,000 and one of 15,000,000 typhoid bacilli. In spite of treatment the ulcer slowly progressed and eventually enucleation of the eye was necessary.

The third case of diplobacillary ulcer, observed and treated by the writer, followed a foreign body removal but diagnosis was made early and treatment begun immediately. The foreign body was above and temporal to the pupillary area and the ulcer therefore started in the periphery and spread centrally. Sulfadiazine was administered orally and topically, the ulcer having been curetted thoroughly before the dusting in of sulfadiazine powder. Healing was complete in four days and there was no loss of vision.

Friedlander bacillus ulcer. The single case of central ulcer due to Klebsiella pneumoniae was in an agricultural worker who received a scratch on the cornea. There developed a slowly-progressing central ulcer, without hypopyon, which responded well to atropinization, curettage, and sulfadiazine orally and topically. Topical applications consisted in iontophoresis with the sodium salt once daily for three days, supplemented by instillations of 5 per cent sulfadiazine ointment every three hours. Healing was rapid, but due to the central location of the ulcer the visual result was poor. The amount of cicatrization was less, however, than would have been expected to result from cauterization.

DISCUSSION

The great preponderance of pneumococcic ulcers in this series was certainly to have been expected. Also to have been expected was the lack of clear-cut clinical signs differentiating the typical (pneumococcic) central ulcer from the atypical (pyocyaneus, streptococcic, diplobacillary, and Friedlander) central ulcer. It should be noted, however, that none of the pneumococcic ulcers showed the slow progression of the diplobacillary and Friedlander ulcers and that, conversely, none of the pneumococcic ulcers had the extremely fulminating character of the pyocyaneus ulcers. A possible further clinical difference between the pneumococcic ulcer and the pyocyaneus ulcer was that the former tended to progress centrally along a rather narrow track while the pyocyaneus ulcer spread out very rapidly to cover the entire cornea. It is of interest also to note that the only ulcers in which hypopyon was lacking were the one Friedlander bacillus ulcer and two of the three diplobacillary ulcers.

In contrast to the difficulty of differentiating clinically among the various etiologic types of central ulcer was the ease with which bacteriological differentiation could be made by means of direct microscopic examination of Gram-stained scrapings. The limited number of bacteria causing central ulcers facilitates their identification and cultures are needed only to confirm the presumptive smear diagnosis. The importance of identifying the infecting organism is self-evident in view of the rapid progress being made in therapy with the antibiotics and sulfonamides.

The role of trauma in the causation of the central ulcers of this series would seem to indicate that damage to the epithelium is a prerequisite to the development of all central ulcers. In this connection it is noteworthy that in the writer's experience a pneumococcic ulcer has never been known to develop in connection with pneumococcic conjunctivitis, even in those extremely severe cases in which secondary toxic iritis has developed. In marginal ulceration of the cornea, on the other hand, trauma plays an insignificant part.

The findings in this series emphasize again the role of solution-bottle contamination in the production of pyocyaneus ulcers. As a matter of fact, solution-bottle contamination is probably much more common than the frequency of pyocyaneus ulcers would indicate. The organism appears to have a particular predilection for solutions of fluorescein and eserine and has been found by the writer in stock bottles of these two solutions in university pharmacies on two occasions. The explanation for the low incidence of pyocyaneus ulcers, in spite of the frequent accidental inoculation of the cornea with the organism, may lie in the experiment of McCulloch,[4] who showed that inoculation of the scratched rabbit cornea never resulted in a pyocyaneus ulcer unless the lids were kept closed after the inoculation. Infection almost invariably took place, however, when the lids were kept closed under a dressing. Prophylaxis would appear to consist in (1) the avoidance of contaminated solutions, (2) the avoidance of dressings after foreign body removal when possible, and (3) the use of an antiseptic ointment in those cases in which a dressing is unavoidable. It should be emphasized, however, that contaminated solutions are not the only possible sources of pyocyaneus ulcers. The organism has been recovered, though extremely rarely, from patients hav-

ing chronic meibomitis, chronic conjunctivitis, and chronic dacryocystitis, and such patients would naturally be potentially liable to pyocyaneus ulcer.

The five bacterial agents found in this series are of course not the only causes of central corneal ulcer but they are certainly the most frequent causes. It is of interest that MacNab,[3] one of the early workers on the bacteriology of corneal ulcers, in his monograph published in 1907, lists the only proven causes of atypical hypopyon ulcer as the streptococcus, the pyocyaneus bacillus, and Friedlander's bacillus. He suggests that Bacterium coli and Aspergillus fumigatus can also produce hypopyon ulcer but later work does not appear to have borne him out. The role of the Diplobacillus of Petit in hypopyon ulcer has now become well established, however, although the number of reported cases[2,5] is small. Central ulcers have been observed by the writer in association with gonococcic conjunctivitis, trachoma, vernal catarrh, etc., but in none of these diseases are they typically central and they have therefore been excluded from this series.

Therapeutic results in this series have convinced the writer that thermal or chemical cauterization of hypopyon ulcers is an outmoded procedure and that proper systemic and topical use of the sulfonamide drugs should serve to arrest progress in all but very exceptional cases. In contrast to the frequency of sulfonamide-resistant strains in such bacteria as the staphylococcus and gonococcus, the finding of resistant strains of beta hemolytic streptococci and pneumococci has so far been rare. Data on the sulfonamide-resistance of Pseudomonas aeruginosa, Klebsiella pneumoniae, and the Diplobacillus of Petit seem not to be available, but an organism related to the Diplobacillus of Petit, i.e., the Diplobacillus of Morax-Axenfeld, is inhibited by sulfathiazole and sulfadiazine and it seems probable that the sensitivity applies to the whole group.

The local application of the sulfonamides in central ulcers is of great importance in obtaining effective concentration of the drug in an avascular tissue. In dermatology and surgery there appears to be a trend against the use of the sulfonamides topically, due, presumably, to local toxic effects and to the frequent development of allergic sensitivity. The work of Bellows,[1] which indicates that the sulfonamides tend to increase cicatrization in abrasions of the rabbit's cornea, must be considered, but from clinical observation it would seem that the human cornea tolerates the sulfonamides, particularly sulfadiazine, very well. Von Sallmann's study[8] of sulfadiazine applied by iontophoresis to the rabbit cornea indicates that the drug is only very slightly toxic.

In the treatment of hypopyon ulcers the writer has had very little experience with penicillin and none as yet with streptomycin, but there is every reason to believe that penicillin will be the preparation of choice in both pneumococcic and streptococcic ulcers, and that streptomycin will be the treatment of choice in pyocyaneus and Friedlander bacillus ulcers. It seems likely that streptomycin will also be found to be active against diplobacillary ulcers although no data to that effect are as yet obtainable. It should be pointed out that there is no contra-indication to the simultaneous use of the sulfonamides and penicillin since their mode of action differs.[9]

SUMMARY AND CONCLUSIONS

1. A series of 50 acute central (hypopyon) ulcers is reported. A presumptive identification of infecting organisms was made on Gram-stained scrapings from each ulcer and was confirmed in each case by culture. Of the 50 cases, 35 were caused by pneumococci, six by beta hemolytic streptococci, five by pyocyaneus bacilli, three by diplobacilli (Petit variety), and one by the Friedlander bacillus.

2. Therapy with oral and topical administration of the sulfonamide drugs, particularly sulfadiazine, was found to be much more successful than older methods of therapy. The value of the antibiotics, particularly penicillin and streptomycin, is discussed.

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Correction

Because of a typographical error in the printing of a formula which was part of "What's New in Endocrinology," an article by George W. Thorn, M.D., which appeared in the June, 1948, issue of CALIFORNIA MEDICINE, the corrected version is printed herewith.

Potassium Phosphate Solution:
K_2HPO_4 2.0 gm. } K=25 m.eq./l
KH_2PO_4 0.4 gm. } P=14mM/l
Glucose 60.0 gm.
q.s. ad. 1000 cc. H_2O
To be infused slowly over a period of two hours.

Benadryl and Pyribenzamine in the Treatment of Diseases of the Skin

Grant Morrow, M.D., *San Francisco*

BENADRYL and pyribenzamine are two new synthetic drugs which have the ability to neutralize the effects of histamine or histamine-like (H) substances which most investigators believe to be identical.

Since Dale and Laidlow[5] pointed out the similarity of anaphylactic shock and histamine effects, numerous methods of specific and non-specific means of combating reactions to histamine have been tried without success. Prior to 1932[11] at least 165 methods or drugs, including sodium thiosulfate, barium salts, non-specific serums and proteins, were tried. In more recent years[8] Vitamin C, barbital, Vitamin P (hesperidin) and ethylene disulfate all have been found to be ineffective or of doubtful value.

Desensitization with histamine itself has not resulted in any success in various allergic manifestations.[7]

Best,[2] in 1929, reported that histaminase would neutralize histamine in vitro, but clinical investigations by many workers, including Best himself in 1940,[3] demonstrated the administration of histaminase has no effect upon histamine spontaneously present in the body or upon that given by injection.

Since histamine itself did not stimulate antibodies, Fell[9] conjugated histamine and horse serum with an azo linkage, called histamine-azoprotein (hapamine). The author's own experience and that of others[6] with injections over many months has shown this compound to be ineffective clinically in many allergic dermatoses.

In 1933 Fourneau and Bovet[10] showed that certain phenolyic ethers have the property of counteracting the action of histamine in vivo and in vitro.

In this country, two compounds have been used, benadryl and pyribenzamine. Benadryl is beta-dimethylaminoethyl benzohydryl ether hydrochloride. Curtis and Owens[4] showed benadryl to control acute urticaria in 11 out of 18 cases (61 per cent). Shaffer[15] reported that seven of eight patients with urticaria had been benefited. O'Leary and Farber[13] reported nine of 15 cases of acute urticaria had been completely relieved and that 25 of 35 patients with chronic urticaria had been almost completely relieved. Other authors have had similar results: 70 to 90 per cent relief in acute urticaria; 50 to 70 per cent relief in chronic urticaria. Side reactions to benadryl are quite common. Sleepiness, dizziness and lassitude occurred in 50 per cent or more of patients, occasionally necessitating the cessation of the drug. Other side effects include dryness of the mouth, nausea and excitement.[17] Slater[16] reported an asthmatic patient, taking benadryl, who became so drowsy that he wrecked an electric platform cargo truck.

Pyribenzamine was first prepared by Mayer, Huttner and Scholz.[12] Pyribenzamine is N'Pyridil-N'Benzyl-N Dimethylethylenediamine. They carried out experimental studies and found the drug to neutralize the effects of histamine, both in vivo and in vitro. Arbesman[1] showed relief of 93 per cent of patients with acute urticaria and relief of 75 per cent of those with chronic urticaria. Feinberg[8] found symptomatic relief in pruritus of acute and chronic atopic dermatitis in 16 of 18 patients. Osborne[14] found 23 of 24 cases of acute urticaria relieved by pyribenzamine and the same percentage by benadryl. Urticaria recurred in six of nine patients cleared with pyribenzamine when the drug was discontinued. In atopic dermatitis, the drug was found to be palliative in two-thirds of the patients. Four patients with dermatitis venenata were given pyribenzamine and three responded favorably.

Side reactions to pyribenzamine are less frequent than to benadyrl. Drowsiness and lassitude occur in 18 per cent; dizziness in 13 per cent; nervousness and insomnia in 10 per cent; dryness of the mucous membranes in 8 per cent and palpitation in 5 per cent. Most of the reactions are mild and do not necessitate the discontinuance of the drug.[8]

CLINICAL STUDIES

In this paper we wish to present the studies of the results of the use of pyribenzamine and benadryl in various skin disorders at the Dermatology Clinic of the University of California Hospital, Southern Pacific General Hospital and in private practice. We used the drugs in a total of 241 cases.

Each drug was always given orally, the dose of pyribenzamine in adults usually was 50 mg. four times a day, and that of benadryl 50 mg. three times a day. In some patients it was necessary to reduce this dose 50 per cent. Occasionally it was necessary to increase the dose of either drug to 100 mg. four times a day. In children the dose was computed according to weight; usually 2 mg. per pound. Benadryl has the advantage in children in that the elixir containing 10 mg. per teaspoonful can be used. Pyribenzamine cannot be used in an elixir because of the marked anesthetic effect on the oral mucus membranes and the tongue.

Penicillin Reactions. (Urticaria, erythema multiforme). Nineteen cases were followed satisfactorily.

From the Department of Dermatology of the University of California Medical School, service of Hiram E. Miller, M.D.

Read before the section on Dermatology and Syphilology at the 76th Annual Session of the California Medical Association, April 30-May 3, 1947, Los Angeles.

Eight of the patients were given pyribenzamine, and in seven the urticaria cleared in two to three days. One patient was not helped. Nine were given benadryl; in seven the urticaria cleared in two to three days, and one patient was not helped. Two patients were given benadryl and pyribenzamine simultaneously without response over a ten-day period.

Atopic Dermatitis. Thirty-seven patients with atopic dermatitis were treated with pyribenzamine or benadryl. Twenty were treated with pyribenzamine over a period of two to six weeks. Three were free of symptoms in one month; 14 were improved and the pruritus was controlled over two to three months; two were not helped. Twelve patients were treated with benadryl with adequate follow-up; four of them were rid of the disease in one month, six were improved and the pruritus controlled in four to six weeks, and two were not helped over a period of six weeks. Five patients were given pyribenzamine and benadryl together; one was improved and four were unaffected. As a rule the drug has to be given over a period of months in order to keep the atopic dermatitis under control. In some patients, taking the drug only at the time of flare keeps the skin clear.

Pruritus Ani and Vulvae. Twenty-seven patients were followed adequately. Seventeen were given pyribenzamine; three were relieved within two weeks, ten were better, and all but four were well within one month. Eight patients were given benadryl and five of them were improved within two weeks, while three were not helped. Both benadryl and pyribenzamine were given in two cases without any effect on the pruritus.

Acute Urticaria and Erythema Multiforme. Thirty patients with acute urticaria and erythema multiforme were treated with benadryl or pyribenzamine. Pyribenzamine was given in 17 cases; in ten there was relief of pruritus in one to two days and it was cleared within five days; in one case it did not help. In 13 cases benadryl was given; the disease was controlled within one to two days in ten cases, the skin was clear within five days. Two patients had relief of pruritus but it took more than five days to clear. In one case, benadryl was of no help. Two patients were given pyribenzamine and benadryl together without effect.

Poison Oak Dermatitis. Twelve cases were adequately followed in this group. In eight the patients received pyribenzamine; in three the skin was clear in one week and the other five there was notable improvement. Benadryl was given in four cases; in one the dermatitis cleared within five days and in two within eight days, while in one it did not help.

Dermatitis Venenata. This group contained patients with various types of dermatitis venenata, including reactions to sulfur, sulfonamide and penicillin ointments, soaps, weeds and the like. There are 37 patients in this group. Thirty-three received pyribenzamine. The pruritus was controlled and there was marked improvement within five days in 29 of them. In four there was no help. Benadryl was given to four patients. Two of them showed definite improvement and relief of pruritus within five days. Two were not helped by benadryl.

Dermatitis Medicamentosa. There were 12 such cases. Ten of the patients received pyribenzamine; in four the skin was clear within five days, and four had relief of pruritus and were improved within five days. Two were treated with benadryl. The skin of one was clear within five days; one was not helped.

Nummular Eczema. There were 13 cases of this disease. Twelve patients were treated with pyribenzamine. In three the skin was clear within two weeks; in seven the pruritus was controlled and there was definite improvement within two weeks, but in two there was no effect. Benadryl was given to one patient, whose pruritus was relieved in two weeks.

Post-Scabetic Pruritus. There were 19 cases. Pyribenzamine was given in 12 cases; six of the patients had clear skins within five days; six were improved and the pruritus well controlled in five days. In seven cases benadryl was given; two were clear within five days; four were improved and the pruritus controlled in five days and one was not affected.

Stasis Dermatitis With Absorption Phenomena. There are 17 cases in this group. Twelve patients were given pyribenzamine; in one the condition cleared within a week; seven showed improvement with the pruritus controlled after two weeks, and four were not helped. Benadryl was given to five; in one case the skin was clear within one week; in three there was improvement with the pruritus controlled after a two-week period; one showed no benefit.

Dermatitis Herpetiformis. Six patients were treated. Four received pyribenzamine for one month. In one there was improvement with relief of pruritus. Three showed no change whatsoever. Benadryl was given to two patients for a month. One showed improvement with relief of pruritus after one month. One was unaffected after six weeks.

Seborrhea. In this group there were seven adequately followed patients. Four were treated with pyribenzamine, all with definite improvement and relief of pruritus. Three were treated with benadryl and improved. Relief of pruritus occurred in two cases. In one there was no effect.

Miscellaneous Group. Two patients with generalized pruritus from jaundice were given both benadryl and pyribenzamine separately for one week without any effect on the pruritus. One patient with neurotic excoriations received pyribenzamine and benadryl separately for one month each without change. Two patients with actinic dermatitis showed no benefit from either pyribenzamine or benadryl, each given over a two-week period.

SIDE REACTIONS

Benadryl. The main side reaction to benadryl is drowsiness and lassitude which occurs in 50 to 60 per cent of patients. Headache occurs in 5 to 10 per cent; nausea in 4 to 5 per cent; excitement in 2 to 3 per cent; urinary frequency, reduction of potency and diplopia in about 1 to 2 per cent. It was ne-

cessary to discontinue benadryl in eight of our patients because of severe side reactions.

Pyribenzamine. The main side reaction to pyribenzamine is also drowsiness and lassitude but this is much less severe than that caused by benadryl. These symptoms occurred in 10 to 12 per cent of our patients. The other side reactions such as headache, nausea, excitement, urinary frequency, reduction of potency and diplopia developed in about the same percentage as with benadryl.

DISCUSSION

Both pyribenzamine and benadryl have a definite place in dermatological therapeutics. Pyribenzamine has a wider range of use than benadryl because of the lesser side reactions. In some cases, benadryl has a better effect because of the sedative action. Another distinct advantage of pyribenzamine is the antipruritic factor which is much greater than with benadryl.

It should be emphasized that in all cases except those of urticaria, erythema multiforme, penicillin dermatitis and dermatitis medicamentosa, other treatment was carried out simultaneously. This included wet compresses, superficial x-ray therapy, bland shake lotions and the like.

Neither benadryl nor pyribenzamine is a cure for anything. They give only symptomatic relief while the drug is being taken. Urticaria, erythema multiforme, penicillin reactions and dermatitis medicamentosa will all clear in a few weeks with no treatment, but the anti-histamine drugs will relieve the symptoms and shorten the time of reaction. With other types of dermatoses such as pruritus ani and vulvae, dermatitis venenata, poison oak dermatitis and the like, the pruritus is relieved, alleviating scratching and insomnia. This gives local therapy a better chance and the dermatitis resolves in less time.

Since no serious side effects, such as blood dyscrasias, jaundice or death, have been shown to date to be due to either benadryl or pyribenzamine, neither drug should be withheld because of fear of severe complications.

CONCLUSIONS

1. Results are presented in 241 cases of various dermatoses treated with pyribenzamine and benadryl.

2. Pyribenzamine is superior to benadryl because of the greater antipruritic element and lesser side reactions.

3. Those dermatoses most helped by benadryl and pyribenzamine include penicillin reactions, pruritus ani and vulvae, urticaria, erythema multiforme, dermatitis venenata including poison oak, dermatitis and dermatitis medicamentosa.

4. The dermatoses helped to a lesser degree include nummular eczema, atopic dermatitis, postscabetic pruritus and stasis dermatitis with absorption phenomena.

5. In our brief experience dermatitis herpetiformis was not benefited.

909 Hyde Street.

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Discussion by James R. Drake, M.D., *San Francisco*

It is admittedly difficult to determine the therapeutic value of new agents such as those under discussion. In general, many workers have continued to use local radiation therapy, dietary exclusions, etc., while at the same time administering benadryl or pyribenzamine. I feel that in practice this is as it should be (outside the realm of pure academic investigation, of course). I would agree that the use of these drugs is palliative and does not relieve the physician of his responsibility for doing an adequate work-up—determining the offending allergens where indicated and taking reasonable measures to eliminate them.

If some of us are disappointed in the results from benadryl and pyribenzamine, it may be because we expected too much. It should be kept in mind that the histamine mechanism is not necessarily the only one in effect in our clinical cases of allergy.

In short, we now have two drugs which if administered with care may give our patients varying degrees of relief. We have, however, no true cure, no panacea, no definite shortcut, no royal road to solution of the allergy problem.

Standards for the Diagnosis of Activity and Inactivity in the Rheumatic State

Harold Rosenblum, M.D., *San Francisco*

THE difficulties which exist in the diagnosis of rheumatic fever are well recognized and have been discussed frequently in the literature. In recent years, the diagnostic spotlight has shifted from the acute and spectacular forms of the disease in young adults, to the insidious, the latent, and the subclinical forms, especially in children. The latter are of greater over-all importance. Lacking a truly adequate clinical definition of the disease, and lacking a specific diagnostic test, the clinician is frequently beset with perplexing difficulties in establishing or ruling out the diagnosis, rheumatic fever. The growth in our knowledge of the natural history of the disease has explained, but has not simplified, the problems in diagnosis.

The course of rheumatic fever varies widely, not only from patient to patient, but in the same patient, from time to time. One cycle may appear to end in a few weeks leaving no obvious sequel; another may overwhelm the patient and quickly cause death; still another may be one of a number of recrudescences characterized by arthritis, fever and advancing cardiac damage. The clinical picture most often witnessed includes recurrences of symptoms and signs alternating with periods of apparent quiescence, especially in the earlier age group.[2] Thus, the diagnosis "rheumatic fever" is clinically inadequate unless it takes into account the concept of activity and inactivity. This concept is prerequisite to the best handling of the patient, for its goal is preventing or minimizing cardiac damage through proper therapy while activity is present and through the prevention of recurrence in the inactive stage.

A useful tabulation of criteria for the diagnosis of rheumatic fever is that of Jones,[7] who separated the clinical features into major manifestations (carditis, arthralgia, chorea, nodules, and verified history of previous rheumatic fever), and minor manifestations (fever, abdominal or precordial pain, erythema marginatum, epistaxis, pulmonary changes and abnormal laboratory findings). He suggested that any combination of the major manifestations, or the coexistence of one major and two minor manifestations would yield reasonably good evidence for the diagnosis. The criteria of Jones and of others[5,16] have helped to define the clinical diagnosis. Recent descriptions of variants[14] and of atypical[13] or subclinical features[10,11] have extended the present limits of the clinical picture. It is not our object here to stress again the considerable problems in diagnosis and differential diagnosis except to keep clearly in the foreground the concept of rheumatic fever as a long-continued process which involves any or all of the tissues of the affected patient, and the manifestations of which are variable—some, such as acute arthritis and valvular heart disease, being obvious; others, such as carditis, often being clinically obscure. The rheumatic process eventually becomes quiescent, and in the inactive stage, chronic rheumatic cardiac disease is the only known remaining sign. Determining when rheumatic fever has reached the inactive phase is one of the most difficult problems associated with the disease, and every aspect, including history, physical signs, laboratory, X-ray, and electrocardiographic data must be considered in diagnosing inactivity.

MATERIAL

The material which forms the basis for this paper is drawn from experiences with patients suffering from rheumatic fever or suspected rheumatic fever seen in the Naval Service (1942-46), in the diagnostic clinics sponsored by the California State Board of Public Health and the Heart Division of the California Tuberculosis and Health Association,[12] in hospital teaching wards and in private practice.

CLINICAL MANIFESTATIONS OF ACTIVITY

Acute carditis is the most important manifestation of activity. It is not only the most frequent, but the most destructive, and it varies from gross, obvious pancarditis to latent, continuing inflammation which is difficult to detect by the most delicate methods now available. It is recognized by tachycardia, variability in heart sounds, rapid increase in cardiac size and in the evidence of valvular involvement, cardiac insufficiency, and acute pericarditis. Taran has pointed out that these signs are inadequate in detecting the milder degrees of carditis.[17,18] He observed that changes in the cardiac rhythm as a result of relative prolongation of systole as compared with diastole will produce a sensitive auscultatory sign of carditis, a kind of tic-tac rhythm, which is independent of the cardiac rate. This can be determined with the electrocardiograph by measuring electrical systole, the Q-T interval. Taran showed that children who were kept at complete bed rest until all evidence of carditis had disappeared (including prolongation of the Q-T time) were better off, as measured by the incidence

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of recurrences and of cardiac enlargement, than were a similar group who were permitted limited physical activities when all evidences of carditis had disappeared except prolongation of the Q-T interval.

Nodules and erythema marginatum are both so closely identified with active rheumatic fever that either can be taken as synonymous with activity. Incidentally, nodules will be found in some patients only if they are carefully searched for, not only in the usal distributions such as the scalp, elbow, and over other bony prominences, but along tendon sheaths and fascial layers any place in the body which is available to inspection and palpation.

Chorea, also, is practically synonymous with rheumatic fever. It is, however, rare in adults,[5] and the full extent of cardiac sequellae may not be detectable for years.

Pneumonitis, acute bronchitis, and acute pleurisy occurring in a rheumatic patient are highly suggestive, but, if they occur in the absence of other signs, are hardly sufficient evidence to indicate rheumatic activity.

"Unexplained" nose bleeds are common in rheumatic children and uncommon in rheumatic adults. If the epistaxis is severe, and sudden in onset, and especially if it is associated with purpura, it is a strong diagnostic point in favor of activity in a known rheumatic. Renal bleeding will occasionally occur in a rheumatic child who also suffers from nose bleeds, and in the absence of glomerular nephritis, cardiac failure or renal infarction.

Migratory polyarthritis, probably because of its obvious and dramatic nature, has been considered the classical clinical manifestation of the disease, and when it occurs in a known rheumatic person can be taken as presumptive evidence of activity. It is relatively more common in the adolescent and young adult groups than in childhood;[2] it is not a constant feature of the disease, however, at any age. Rheumatic activity cannot be positively diagnosed from arthritis alone; in fact, when polyarthritis is rheumatic, other evidences will also be found. Moreover, persistent arthralgia and muscular pain may extend into the inactive stage of the disease.

Fever in rheumatic patients is ordinarily present during the beginning of a rheumatic cycle when other obvious signs of activity are also present, and it ordinarily disappears, especially if salicylates are administered, long before rheumatic activity has subsided. Low-grade fever, especially in apparently healthy children, and particularly if it occurs after exercise, is not to be taken as an indication of illness when it is an isolated finding.

Loss of weight or failure to gain is rather common at the onset of rheumatic fever or at the beginning of a cycle of activity, but a restoration of the body weight to normal is not necessarily indicative of inactivity for, like temperature, a return to normal may precede by long periods the return to the quiescent period.

Acute abdominal pain is not uncommon in rheumatic children, and not very rare in rheumatic adults. It is frequently difficult to decide whether it arises from acute serous peritonitis, from hepatic enlargement, from acute perisplenitis or acute pericarditis, from pleurisy or from some non-rheumatic source; for example, acute appendicitis. Other evidence is required before abdominal pain can be interpreted as a sign of rheumatic activity.

The pulse rate is considered to be characteristically elevated in acute rheumatic fever, and the elevation is disproportionately high as compared with temperature. Like fever, the pulse may return to normal while activity is still present; however, in such instances, the increment in rate with exercise or emotion may be unusually great or more sustained than in normal persons or in quiescent rheumatics. Slow pulse rates are found during rheumatic activity with second and third degree heart block and with A-V nodal rhythm. In young adults at least, sinus bradycardia and exaggerated sinus arrhythmia are occasionally observed with acute carditis.

LABORATORY MANIFESTATIONS OF ACTIVITY

The sedimentation rate is characteristically elevated in acute phases of rheumatic fever[3,14] and constitutes a useful laboratory test for activity. In no sense, however, should it be considered as a specific diagnostic test. It has the following disadvantages as a guide to the presence of activity: (1) It may be altered by salicylates, cardiac failure, anemia, or by concomitant but independent infections; (2) It may return to normal while rheumatic activity is still present;[18] (3) It may continue to be elevated after activity has ceased.[18]

Secondary anemia is a common finding in the acute rheumatism of children[6] but not in adults,[14] especially when milder forms of the disease are considered.[5]

Leukocytosis is an untrustworthy sign of rheumatic activity since it is usually of relatively short duration and may be absent entirely during the most acute periods.

Reduction of the vital capacity is a useful sign of rheumatic carditis which it measures indirectly through the measurement of left ventricular failure.[19] It is a sensitive test, but has the disadvantages of being unsatisfactory for use in small children and in patients with valvular heart disease and cardiac enlargement whose readings, even in the absence of activity, would be reduced.

X-RAY CRITERIA

The sudden development of enlargement of all or part of the heart with acute carditis can be observed by x-ray. Occasionally, localized or diffuse dilatation of the aorta or pulmonary artery will be seen during rheumatic fever and will constitute positive evidence of activity in a case which might otherwise be doubtful.

ELECTROCARDIOGRAPHIC CRITERIA

Although the electrocardiogram does not constitute a specific means of diagnosing rheumatic carditis, varying degrees of A-V block are classical and are sufficiently characteristic to be of great diagnostic value. Alterations in the contour of any of the in-

dividual waves (P,[13] QRS and T[15]) and in the S-T segments[9] are not rare. When precordial leads are taken[1,8] the frequency of abnormal findings is increased. Ectopic beats, A-V nodal rhythm, shifting pacemaker, exaggerated sinus arrhythmia, paroxysmal auricular tachycardia, auricular fibrillation and the characteristic electrocardiographic pattern of pericarditis may be found.[4] Generally speaking, there will be a direct proportion between the number of films recorded and the number of abnormalities observed. Serial records may be significant, as in myocardial infarction, merely by showing changes from one record to the next. At the same time, the clinician should be prepared to find an occasional case in which electrocardiographic abnormalities have become permanently fixed, although the rheumatic fever has become inactive.

Taran has made careful measurements of the duration of electrical systole in rheumatic children and concluded that it is prolonged significantly in all cases of rheumatic carditis.[17] The prolongation found by him was a function of the severity of the carditis and not of the cardiac rate. From limited personal experience with this criterion of activity, we believe it to be valuable in the diagnosis of active carditis in children.

The various manifestations of activity are shown in order of their probable significance in Table 1.

Table 1.—*Clinical Manifestations of Activity in Rheumatic Patients, Other Causes Excluded, Grouped in Order of Significance*

Activity Positive	Activity Probable	Activity Suspected
Carditis (including electrocardiographic evidence)	Arthralgia and Myalgia	Fever
Nodules	Pneumonitis, Acute Bronchitis, Acute Pleurisy	Weight loss
Erythema Marginatum	Increased Sedimentation Rate	Abdominal and Chest Pain
Chorea	Reduced Vital Capacity	Rapid Pulse
Polyarthritis		Anemia
		Leukocytosis

RELATIVE INCIDENCE OF ACTIVE AND INACTIVE CASES

The frequency with which active and inactive cases are found amongst rheumatic persons will vary with many factors. Activity will be found more frequently in the younger age groups, particularly children, for then the disease is most active and severe, and recurrences are more common than they are after puberty.[2,20] Active infection will be found most often in those who have had known rheumatic activity in the recent past. The risk of recurrence for the year immediately following an attack, according to Wilson, is 38.7 per cent as compared with 11.2 per cent in the year immediately following one year of freedom from a recurrence.

Activity will be found in proportion to the care with which it is sought, and cannot be definitely excluded in a rheumatic-susceptible unless all criteria for its presence are applied and found negative.

Table 2.—*Diagnosis Summary for Seven Hundred Children Receiving Care Through the Rheumatic Fever Demonstration Program*
Selected Areas in California,* 1940-46

Etiology	Number	Percent
TOTAL	700	100.0
Active rheumatic	110	15.7
Inactive rheumatic	289	41.3
Congenital (without R.F.)	44	6.3
Non-rheumatic	102	14.6
Unknown	155	22.1

*The demonstration program was carried out in Solano and Contra Costa counties, with a few children admitted from nearby areas.

During the years 1940-46, facilities for the diagnosis of rheumatic fever were made available in a special clinic for the children of Solano and Contra Costa counties. Of the first 700 children who were referred, 155 were not considered to have received enough study for a final diagnosis and 545 were considered to have been investigated adequately. Of the 545, 399 were diagnosed as having rheumatic fever or rheumatic heart disease, and, of the rheumatic group, 110 were considered active and 289 inactive. Congenital cardiac disease was diagnosed in 44. This is shown in Table 2. Thus, with reasonable, although not necessarily exhaustive examinations (including medical history, physical examination, cardiac fluoroscopy, electrocardiogram, sedimentation rate and blood count), 399, or 73 per cent, of 545 children referred to a cardiac diagnostic clinic were found to be rheumatic, and 27.5 per cent of the rheumatics were in the active stage. The importance of detecting the presence of activity in these 110 rheumatic children is obvious, since for all of them treatment was recommended, and for many of them provision was made for carrying it out.

SUMMARY AND CONCLUSIONS

1. The diagnosis rheumatic fever is inadequate for clinical purposes unless it carries with it the concept of activity and inactivity.

2. Various manifestations of rheumatic activity and the difficulties in their interpretations are reviewed, and suggestions for their clinical applications are summarized.

3. The relative incidence of rheumatic fever and heart disease, resolved as to activity and inactivity, in an ambulatory group of 700 California children who were referred to a public diagnostic clinic is reported.

450 Sutter Street.

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Treatment of Superficial Fungus Infections in Routine Dermatologic Practice

Rees B. Rees, M.D., *San Francisco*

Peck and associates[10,11] first reported the effectiveness of sodium propionate and of a mixture of fatty acids in dermatophytosis. Fatty acids were first used by the baking and dairy industries as inhibitors of molds. Keeney and his coworkers[2,3,4,5] have recorded excellent clinical results with the soaps of propionic, undecylenic and caprylic acids and have concluded that caprylic is the most effective. From the clinical point of view, however, there appears to be no outstanding superiority of one of these agents over the others. Various authors[8,13,14,15] have published favorable reports on undecylenic acid compounds. One study in particular[16] indicated that undecylenic acid and its zinc salt are especially effective in prophylaxis of foot infections. Our experience with fatty acids has been confined almost entirely to the use of 5 per cent undecylenic acid and 20 per cent zinc undecylenate in a special ointment base ("Desenex" ointment—Wallace and Tiernan Products Incorporated, Belleville, New Jersey). Another preparation which we have used only in treatment of tinea capitis is 5 per cent salicylanilide in Carbowax ("Salinidol"—Doak Company, Cleveland, Ohio). Our interest in this compound was aroused by the favorable report of Schwartz et al.,[12] who used it in controlling an epidemic Microsporum audouini infection of the scalp.

From the Department of Dermatology of the Division of Medicine of the University of California Medical School.

DERMATOPHYTOSIS OF THE FEET

The need for an effective agent which could be dispensed without special precautions led to an extensive study during the war at Fort Benning, Georgia. Hopkins et al.[1] found a high percentage of clinical cures among patients treated over four weeks with preparations of undecylenic acid and its salts. The effect was often slow. In the first two weeks of treatment the percentage clinically clear and the percentage relieved of itching was no higher than the percentages achieved with other agents. However, the incidence of irritation was lower than in any other large series. Several powders were tried and found to be relatively ineffective but other authors have reported favorably on the use of more highly concentrated undecylenic acid powder. Solutions in water,

alcohol and propylene glycol proved more rapidly effective in some patients but were not well tolerated in fissured and denuded lesions.

Keeney[6] felt that fatty acids preparations have a distinct advantage in that they are antiseptic as well as fungistatic. He believed that an ointment containing propionic acid and sodium propionate was as effective clinically as the undecylenic acid ointment for involvement of the feet, the groin and the smooth skin and that either preparation is an improvement over any agent previously employed. It was his opinion that in this respect the treatment of dermatophytosis has been standardized.

Fatty acids higher in the series than undecylenic have been tried clinically on a small scale but no conclusive results are yet available. Hopkins' group also tested several familiar fungicides, including salicylic acid in combination with sulphur, benzoic acid, tincture of merthiolate, and iodine. They stressed the likelihood of disabling dermatitis from their use. However, the concentration of the active ingredients was greater than in the fungicides customarily employed by us. For example, salicylic acid concentrations varied from 3 per cent to 12 per cent, whereas we do not exceed 1 to 2 per cent except for hyperkeratotic involvement. Similarly, sulphur was used in a 10 per cent concentration in ointment form, whereas we prefer to use concentrations no greater than 3 to 4 per cent.

Analysis of 110 cases of dermatophytosis of the feet indicated some general trends, although this series is too small for comparison with such large scale studies as that of Hopkins' group. Practically all our patients were given superficial fractional doses of roentgen therapy because they had relatively severe or resistant types. Forty-seven were treated with a starch lotion containing 5 per cent liquor carbonis detergens. Of those patients, 85 per cent obtained symptomatic relief within two weeks, and 21 per cent were clinically well within a month. Thirty-five patients were given 5 per cent undecylenic acid and 20 per cent zinc undecylenate in a water miscible base, with 77 per cent symptomatically relieved in two weeks and 40 per cent clinically cured within a month. There were two cases of irritation in this group. Thirty-three were treated with 40 per cent alcohol containing approximately 2 per cent salicylic acid and 4 per cent benzoic acid, with 82 per cent symptomatically relieved within two weeks and 36 per cent clinically well. Three had irritations.

Other agents used included 0.5 per cent aluminum acetate solution, 2 per cent crude coal tar paste, potassium permanganate solution, etc. Sixty-nine persons were treated with one of these agents, of whom 87 per cent obtained symptomatic relief within two weeks, and 30 per cent were clinically well within a month. Two in this group had unfavorable reactions.

In this small group of relatively resistant cases the undecylenate-undecylenic acid preparation, as a representative of the fatty acid series, had no advantage in providing rapid symptomatic relief, but did produce clinical cures in a slightly larger proportion than other agents. However, it was not spectacularly superior to other compounds when used for a period of a month or less. Hopkins[1] emphasized that although the percentage of satisfactory results was higher and irritations were lower than with other agents, these differences were not great. He also pointed out that the advantage of fatty acid preparations became more evident only after a month's treatment. In a group of 509 cases treated with undecylenic acid preparations and followed for less than a month, there were only 43 per cent clinical cures, whereas there were 70 per cent clinical cures in 292 cases observed over four weeks.

Quite often the role of the fungus infection is relatively unimportant, and treatment must be directed toward eczematization, hyperkeratosis, superimposed dermatitis or secondary infection. Fatty acid preparations do not seem to have any advantage in the treatment of the occasional extremely resistant case.

DERMATOPHYTOSIS OF THE BODY AND GROIN

Hopkins et al.[1] found that undecylenic acid preparations frequently caused discomfort when applied to the inguinal fold and to the smooth skin. We have seen occasional irritations from their use in these areas. We have had little or no experience with propionic acid preparations, but they are said to be well tolerated. In our limited experience the undecylenic acid ointment was not as satisfactory as one containing 1 per cent salicylic acid and 3 per cent sulphur in water and Aquaphor (cholesterolized petrolatum—Duke Laboratories).

TINEA CAPITIS

The present American pandemic became apparent in 1943. We became aware of its existence in the San Francisco area in early 1944. The San Francisco Department of Public Health recorded 717 cases in 1945. The number dropped to 616 in 1946, and 124 cases were reported in the first three months of 1947. Cultures performed in the mycology laboratory of the University of California Medical School from May, 1944, to May, 1946, disclosed 113 M. audouini, 58 M. lanosum and three T. gypseum infections.

Analysis of 142 cases treated by us indicated the presence of M. audouini in 130, and of M. lanosum in 12. Boys comprised 103 members of the group, and there were 25 girls. The majority had multiple patches throughout the scalp. When single patches occurred, they were usually on the occiput. Kerion was occasionally seen, and generally preceded an early cure. Irritation was rarely encountered, even though medication was used routinely following roentgen irradiation in epilating doses.

In the group of 130 patients with M. audouini infections, 20 were lost from observation. In the remaining 110, 85 per cent were cured by one of several means. The hair was cropped closely and was kept short throughout the treatment period. The ointment was massaged over the entire scalp twice daily, and the area was washed with soap and water prior to examination under the Wood light (filtered

ultraviolet) at intervals of two or three weeks. Absence of fluorescence on two successive occasions under this light was indicative of cure. Manual epilation was used when practical. A Westinghouse Purple-X 250-watt lamp used by some parents was helpful, but this inexpensive substitute for the Wood light was inadequate in detecting faintly fluorescent hairs.

Special interest was taken in attempts to cure M. audouini infections by conservative means. Schwartz and coworkers[12] were able to cure 56 per cent, their most effective remedies being 5 per cent salicylanilide in Carbowax 1500 and saturated solution of copper undecylenate in the same base. Livingood and Pillsbury[7] reported cures by topical applications in one-third of cases studied. Less successful results were reported by J. Lowry Miller et al.,[9] using several preparations containing propionic acid and its derivatives, as well as some containing undecylenic acid. They were able to cure only about 10 per cent.

In our group, 22 were treated with the 5 per cent salicylanilide ointment, with 55 per cent cures in an average treatment period of two months. Less successful results were obtained in a group of 52 children treated with the undecylenate-undecylenic acid ointment. Only 19 per cent were cured in an average of four months. The failures with both of these preparations were apparent after an average of two months. The largest percentage was cured with roentgen epilation. Of 79 so treated, 84 per cent were cured, fluorescence being absent under the Wood light in an average of two months following radiation. It must be emphasized that the technique of roentgen epilation be left to those especially trained in its use.

SUMMARY AND CONCLUSIONS

1. Fatty acid preparations, of which the undecylenate-undecylenic acid ointment is an example, are useful in the treatment of dermatophytosis.

2. They are relatively free from irritating effects.

3. They possess no clinical advantage over a 1 per cent salicylic acid, 3 per cent sulphur ointment in the treatment of dermatophytosis of the groin and body.

4. The resistant type of epidemic ringworm of the scalp was cured in approximately 55 per cent of cases with the use of 5 per cent salicylanilide in Carbowax 1500 ("Salinidol"). Less successful results were obtained with 5 per cent undecylenic acid and 20 per cent zinc undecylenate in a water miscible base ("Desenex"). In this group approximately 19 per cent were cured. Roentgen epilation accounted for approximately 84 per cent cures in children treated by this method.

5. M. audouini infections of the scalp should receive a two months' trial with 5 per cent salicylanilide in Carbowax (or some equally effective preparation) before roentgen epilation is used.

Discussion by J. Walter Wilson, M.D.

The vast majority of the lay public, an even larger proportion of the medical profession, and perhaps all of those specializing in dermatology most sincerely desire a simple answer to the simple question, "What is the best treatment for athlete's foot?" It must be crystal clear to all of you that such a panacea can never be made available; its advent is rendered impossible by two tremendous obstacles and a host of lesser ones. Of primary importance is the absolute necessity of determining accurately the degree of acuteness of the disease in the individual patient and of predicting efficiently the ability of that particular skin in that particular area to tolerate medication. Secondarily, it is always necessary to keep in mind that no fungicide can kill a fungus with which it does not come into contact and that various mechanical barriers to such contact are always present in all fungous infections to a greater or lesser degree. Additional factors such as the specific causative organism involved, complications in the form of other infection or disease, the degree of added dermatitis present, hypersensitivity to fungous products and individual host resistance must also receive due consideration.

The interaction of so many variable factors renders the services of an astute clinician indispensable in many cases of fungous disease. In all statistical studies the clinical ability of the physician making the study must be taken into consideration, else the tyro will be disappointed when he fails to achieve the same results. Dr. Rees has given us ample evidence that he is an excellent clinician; he has utilized this ability in selecting the treatment for each case and in varying the medication as may have been indicated.

It is to be expected that if an astute clinician obtains a certain percentage of good results with a certain medicament, one less well trained will achieve a lesser figure. I agree with Dr. Rees that fatty acid preparations are useful at times in subacute tinea pedis and that they are less likely to produce irritation than other common medicaments. I have not had good success with these materials in the more resistant and chronic forms. I believe that the slight degree of acidity produced by these fatty acids plays a part in their efficiency and permits their being tolerated in the more acute phases of dermatomycoses where other fungicides produce irritation. Perspiration, containing as it does fatty acids, is slightly acid when first produced and then possesses some fungicidal activity. It is likely that bacterial splitting of urea into ammonia in old perspiration overshadows this slight acidity and explains the increased incidence of tinea pedis with the advent of summer weather. A denuded area which is exuding serum is also alkaline. Applying fatty acids to such areas as these is of assistance in restoring the normal slight degree of acidity under which skin functions best. Some fungi have the ability to change the medium in which they grow toward the alkaline side which they prefer. Fatty acids act as buffers to prevent the occurrence of such change.

It is also noteworthy that all potent fungicides in general use are slightly or more strongly acid in reaction. The list includes all derivatives of phenol, iodine and sulfur. This fact represents more than simple coincidence, in my opinion.

In reference to tinea capitis it cannot be overemphasized that the primarily important factor is mechanical. Many fungicides are available which are capable of killing any species of microsporum rapidly and completely on contact. The problem is that of causing adequate penetration of the medicament into a follicle which is tightly plugged with a hair shaft and its mantle of fungus spores. No medicament so far available can adequately perform such penetration while the affected hairs are *in situ* and cure is finally attained either because of the spontaneous epilation which occurs in some patients with any type of infection, or the employment of artificial epilation by means of forceps or x-radiation. The patient is cured because the infected hairs fall out or are mechanically removed, not because of the excellence of the fungicide selected. Any one of a number of fungicides will

then suffice, principally by preventing reinfection in new areas and sterilizing the patulous follicles while the new hair grows. The vehicle called "Intraderm" was designed to penetrate intact follicles containing hairs to the greatest possible degree. Fortified with a selected fungicide (TCAP, trimethyl cetyl pentachlorphenate) it has yielded good results in the hands of its inventors. My experience with this material has been encouraging to date although not as good as previous reports would indicate. Salicyl-anilide is, in my experience, a very good medicament for the treatment of tinea capitis.

Discussion by A. Fletcher Hall, M.D.

Without criticizing Dr. Rees for not performing microscopic and cultural tests in the handling of superficial fungus infection in routine dermatologic practice, I do wish to point out that it is impossible properly to evaluate the comparative results obtained by various methods of treatment without such mycologic studies. Furthermore I do not believe it proper to draw any conclusions regarding the relative efficacy of several methods of treatment when all of the patients have received roentgen therapy in addition to the treatment methods being evaluated.

It is entirely possible that an important percentage of the cases in Dr. Rees' first group (where about 20 per cent cures were obtained following treatment with a Liq. Carbonis Detergens shake mixture—and x-ray) may have been a non-mycotic dyshidrosiform eruption; this is also true of the last group in which healing followed the use of various non-specific methods of local treatment (plus x-ray). If the infection in a large percentage of these two groups were non-mycotic while the infection in a large percentage of the groups treated with fungicides were in fact mycotic, the efficacy of the fungicides then would be shown to be relatively greater. Although I hold no brief for the higher fatty acids, I do not believe that they have been given a proper evaluation in the series just reported.

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An Evaluation of Infertility Factors

Edmund W. Overstreet, M.D., *San Francisco*

DURING the war our study and treatment of infertile couples was much interfered with. So many people changed residence so often that systematic observation and therapy was almost impossible. Moreover, the greatly increased birth rate tended to focus the attention of the obstetrician-gynecologist more on the problem of coping with this reproductivity than on that of enhancing it. But now that the youth of this country is again free to undertake familial responsibilities, our offices and clinics are increasingly besieged by barren couples. This is, therefore, an opportune time for us to take stock of our knowledge in this field and to re-evaluate our techniques for the study and treatment of infertility.

Experienced workers in the field of infertility have made various classifications of the factors which play an etiologic role. In general they are agreed on five principal groups of such factors. These are listed, not in the order of their importance, but in the order of their consideration here.

1. The Coital Factor
2. The Male Factor
3. The Tubal Factor
4. The Female Endocrine Factor
5. The Cervical (and Vaginal) Factor

For a more extensive classification of these groups—correlated, moreover, with diagnostic and therapeutic procedures—attention is called to the excellent one which forms the basis of the brief paper by Page and Page[6] on "An Outline For The Office Investigation of Sterility."

Each student of infertility accords a certain significance and emphasis to each major group of factors. The various opinions are often widely divergent. Our aim will be to cast a little light on the relative importance of these factors, and to attempt to point out where there has been overemphasis and where there may have been insufficient attention. There is not space for even an adequate discussion of specific diagnostic and therapeutic methods, but certain of them have been selected for mention because of common misconceptions concerning them.

THE COITAL FACTOR

Let us touch only briefly on this factor. That is not, however, to underestimate its importance. In general, a simple but searching coital history plus a post-coital, Hühner test will give us an adequate knowledge of the role it plays in the infertility of any couple. But we have all had the painful experience of being deceived by an occasional wife who at the outset has given a history of what seemed to be satisfactory sex adjustment, only to discover on later and deeper probing that male impotence, dyspareunia, infrequent coitus, or unannounced coital techniques played a real part in the couple's infertility.

It is in the relationships of this factor, also, that we have made a beginning in the direction of giving due weight to the psychosomatic factor in infertile couples. What part satisfactory sex adjustment plays, for example, in the physiology of reproductive tract secretions is as yet obscure, but we begin to suspect that we cannot ignore it in carrying out a complete infertility study. The determination of the degree and extent of psychic influence on the reproductive soma represents an almost totally unexplored field of which we are just becoming aware, one which may repay us well for our study of it.

We all know, on the other hand, how frequently pregnancy occurs as a result of the most inept coital techniques. The following factors in our list are certainly much more significant in the problem of infertility.

THE MALE FACTOR

This factor in childless couple does not even now receive the attention it deserves. This is true in spite of the fact that extensive study by specialized workers has vastly increased our understanding of it. Moreover, there is surprisingly good agreement in the literature on how frequently it is the paramount defect in infertile couples. Almost all studies place its incidence in this respect at between 30 and 40 per cent. The casual physician, called upon to explain infertility, unfortunately is not fully aware of this possibility.

That *the male factor* is widely ignored, was forcibly brought home to many of us during army service as we moved from one station to another in this country, attempting to do a small amount of infertility work on army dependents in addition to other duties. It was heartbreaking to encounter the amazing number of young wives who had undergone fairly extensive sterility studies—even major operative treatment—without a spermanalysis ever having been required of their husbands. It was equally discouraging to find that many of these wives thought that their husbands had had adequate semen analysis—when in reality all that had been done was to glance quickly through a microscope to see if motile spermatozoa were present in the semen.

It is true that our present methods of spermanalysis leave much to be desired. They have been likened to trying to determine the character of a person by looking at him from the top of a tall building as he circulates in a mob of people on the street below. Actually, of course, we *can* tell a good deal about individuals in a mob by observing the behavior of the mob itself. The same is true of spermatozoa. By correlating the characteristics of the mob of sperma-

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From the Division of Obstetrics and Gynecology, University of California Medical School, San Francisco, California.

tozoa with actual male fertility we reach an indirect estimate of the fertility of the individual fertilizing sperm. The more carefully we observe the sperm mob —the semen, that is—the more satisfactory the correlation becomes. Authorities now agree that simply determining the presence of motile spermatozoa in semen is not a satisfactory criterion of fertility—so the brief glance down the microscope is no longer enough. A minimum analysis should certainly include:

1. The physical characteristics of the semen: Volume, viscosity, and presence of abnormal contents.
2. A careful sperm count.
3. A properly stained differential count of abnormal forms.
4. An accurate estimate of percent of motile sperms at various intervals of a 24-hour period (at room temperature).

Such a semen analysis may well eliminate a long and fruitless search for infertility factors in the wife and lead instead to simple treatment of the husband with early resultant pregnancy. Certainly there is no need to emphasize this important point for the present reader.

FEMALE INFERTILITY FACTORS

We come now to discussion of the etiologic factors present in the female. Table 1 presents a collection from the recent literature of incidence figures for the three important groups of factors. It serves to emphasize the areas of certainty and uncertainty in our present knowledge.

THE TUBAL FACTOR

Note that the reports on incidence of *the tubal factor* in infertile women are rather consistent. It plays the major role in 40 to 50 per cent of cases. Thanks to the intensive work of such men as Rubin and Cary the physiology and pathology of this factor are quite well understood. The techniques for studying and treating tubal dysfunction have been so well presented in recent publications[3,9,11] that discussion of them here is not necessary.

One word of warning however should be said. Too many physicians make a final decision regarding the tubal status after only a single tubal insufflation or hysterosalpingogram. The relative merits of the two methods would be too lengthy a topic for discussion here; but it has been well demonstrated by Sharman[9] that a single test with *either* method is subject to about a 10 per cent error. While this error can only be eliminated by repeated tests it can often be reduced by the use of anesthesia, a sedative, or an antispasmodic when the test is performed.

TABLE I

INCIDENCE OF ETIOLOGIC FACTORS IN FEMALE INFERTILITY

AUTHOR	NUMBER OF CASES	CERVICAL FACTOR		TUBAL FACTOR	ENDOCRINE FACTOR
		DEEMED PRESENT	ACTUAL LESIONS		
MAZER & ISRAEL[8]	695	32%		55%	35%
NICODEMUS & RITMILLER[11]	76		4%	50%	69%
WINSON[26]	257	38%		54%	52%
SIEGLER[21]	410	38%	32%	51%	59%
GUERRERO[2]	438	11%		31%	16%
McLANE[9]	372	23%		13%	14%
SHARMAN[19]	500			38%	
THIS SERIES	50		70%		

TABLE II

INCIDENCE OF OCCASIONAL ANOVULATION IN INFERTILE FEMALES

AUTHOR	NUMBER OF CASES	METHOD OF DETERMINATION	INCIDENCE OF ANOVULATION
KOTZ & PARKER[6]	47	ENDOMETRIAL BIOPSY	36%
ROCK, BARTLETT, & MATSON[17]	392	ENDOMETRIAL BIOPSY	9%
NOVAK[12]	39	ENDOMETRIAL BIOPSY	49%
JEFFCOATE[5]	63	ENDOMETRIAL BIOPSY	25%
EFFKEMANN[1]	81	ENDOMETRIAL BIOPSY	14%
HALBRECHT[3]	130	BASAL BODY TEMPERATURE	12%
MAZER & ISRAEL[8]	695	BASAL BODY TEMPERATURE	15%
WINSON[26]	257	BASAL BODY TEMPERATURE	35%
McLANE[9]	372	BASAL BODY TEMPERATURE	14%
SHARMAN[19]	500	BASAL BODY TEMPERATURE	6%
ZONDEK[27]	2000	MIXED	11%
COMBINED SERIES	4576	ALL	13.3%

THE FEMALE ENDOCRINE FACTOR

One aspect of *the female endocrine factor* that has received great attention in recent years is the study of defective oogenesis by the determination of anovulatory menstrual cycles—or, if you will, pseudomenstrual cycles. Many workers have placed great emphasis upon absence of ovulation as an infertility factor, and have devoted endless time to devising methods for the hoped-for stimulation of ovulation. But *is* this an important factor in female infertility in general?

Morton and Hayden,[4] gave us a good baseline for the consideration of this problem. They showed, by means of endometrial biopsies, that in apparently normal women, having normal menses, under the age of 40, who had had one or more pregnancies, the incidence of one or more anovulatory cycles over a moderate period of time was about 7 per cent. In similar normal women, not taking the question of previous pregnancy into account, they found the incidence of occasional anovulatory cycles to be about 12 per cent.

What is the incidence in infertile women?

Table 2 presents a collection of figures from the literature. These figures represent the findings of various investigators in terms of what *they* considered to be a *significant degree* of anovulation. Consequently, too much weight cannot be given to them, because the criteria for a significant degree of anovulation are not the same for different workers. Indeed, it is probable that all menstruating women at one time or another have one or more anovulatory

cycles. At just what point such cycles become frequent enough to be a factor in infertility is difficult to decide, and many of the authors in the literature do not state their criteria for making such a decision. The figures of Table 2, however, represent the decisions of respected workers in this field, and as such should carry a certain weight. As quoted, each figure represents the percentage of infertile women in whom it was felt that anovulatory cycles were frequent enough to play a major role in their infertility.

Note the marked divergence of opinion regarding the incidence of significant anovulation in infertile women. One series runs as high as 50 per cent, another as low as 6 per cent. Whether the difference is due to sampling error or to interpretation of the methods used for determination of ovulation is difficult to say; doubtless both factors play a part. If, as seems likely, the former is the more important factor, we can get a better—though still very rough—idea of the true incidence by properly combining these series, using, that is, each percentage figure applied to the corresponding number of cases.

This gives us a total of 4,576 infertility cases with an overall incidence of anovulation of 13.3 per cent. While this figure is twice that for normal women who have borne children, 7 per cent, it is not significantly higher than that for normal women without regard to pregnancy, 12 per cent.

Yet an inordinate amount of attention is being directed to the treatment of this factor in infertile women. So far we have not been able to devise a proven method for direct, immediate stimulation of ovulation. Perhaps this very frustration entices us into redoubled efforts to solve the problem. But should the quest for such a method overshadow study of the other infertility factors?

There is another aspect of *the female endocrine factor* on which we might well dwell for a moment. In certain infertile women we tend to make a rather doubtful assumption. If other sterility factors have been ruled out and if the woman manifests a mild endocrine dysfunction—pituitary, thyroid or ovarian—we are likely to conclude that the endocrine dysfunction is the *cause* of the infertility. In the case of thyroid dysfunction the evidence for this causal relationship is rather good. In the case of pituitary and ovarian dysfunction the evidence is very tenuous. Where such an endocrine upset can be directly related to the occurrence of frequent anovulatory cycles—and where correction of the upset restores ovulation—we are on safe ground. But where ovulation is not in question, to assume that mild pituitary or ovarian dysfunction means the production of infertile ova is very dubious logic. Our knowledge of the physiology of the human ovum is too incomplete to support such reasoning.

What is more important is that this type of thinking may lead to a preoccupation with endocrine therapy which is out of all proportion to its importance and which may turn our attention away from the search for more likely infertility factors.

Both of the foregoing facts are, I think, implicit in the marked disagreement among various authorities regarding the incidence of *the female endocrine factor* in infertile couples. Table 1 shows this clearly.

Nevertheless, the therapeutic approach to infertility with pituitary extracts, chronionic gonadotropins, and ovarian hormones in various dosages and schedules has been labored to the point of absurdity. In conscientious and knowing hands the use of hormone therapy of this type has progressively decreased. Unfortunately, in the therapy of physicians in general its use has steadily increased. Such hormones are now frequently being given purely empirically. They are being given unjustifiably. They are being given irrationally. In some cases they are being given to the definite detriment of the patient. Even a brief comparison of reports in the literature will demonstrate that the percent of pregnancies obtained by those physicians who employ little hormone therapy other than thyroid extract is just about the same as that obtained by those who overdose their patients with all the newest products of the pharmaceutical manufacturers.

THE CERVICAL (AND VAGINAL) FACTOR

Unfortunately, dependence on hormone therapy is often at the expense of attention to the least understood but perhaps most hopeful infertility factor, *the cervical factor*. One is much concerned, for example, when it is realized how many physicians carry out prolonged infertility studies and intensive endocrine therapy without ever performing a post-coital, Hühner Test. Yet it is an indispensable aid in pointing to cervical and vaginal pathological changes of such minor degree as to be difficult of direct observational diagnosis though great enough to be a barrier to spermigration.

That such minimal pathological changes may play an important infertility role is suggested by Siegler's recent paper.[12] He presented 106 cases of infertility in whom study revealed no specific cause and usual treatment methods failed. When a pre-coital douche of Ringer-glucose solution was prescribed for use at the time of ovulation, 29 of these couples conceived. Twenty-seven per cent success is a laudable figure for any type of infertility treatment, and it is to be hoped that sampling error did not enter into it too greatly, or that previously-used treatment did not pave the way for final success. However, in our own last 50 cases of infertility three patients conceived with no treatment whatever other than the pre-coital use of Ringer-glucose solution. One of these three had been infertile for two years but became pregnant at the first ovulation with which the treatment was used.

Whether such a therapeutic result represents a direct effect on cervical and vaginal secretions or whether it represents a stimulation of slightly-below-par spermatozoa is not yet clear; doubtless both factors are involved. Moreover, we are all familiar with the fact that a small percentage of patients become fertile simply as the result of using a therapeutic douche for a short time—and the question of sperm stimulation does not enter here. In any event, present evidence suggests that the beneficial effect

of such therapy so far as secretions are concerned is exerted principally upon those of the cervix, and that artificial alteration of vaginal secretions is of minor importance. That is our reason for classifying *the vaginal factor* only parenthetically with *the cervical factor.*

It may well be that in our routine pelvic examination of infertile women we overlook mild degrees of cervical or vaginal pathological change—or that we have not yet devised adequate methods for detecting them. With regard to the latter, we should cite the important basic work on the physiology of the cervical mucus carried out by Lamar, Shettles, and Delfs[2] and its recent further development by Pommerenke.[7,13,14] Further investigations of this sort are certain to give us more adequate techniques for the study of *the cervical factor* in infertility.

Table 1 suggests how poorly understood—and perhaps how frequently overlooked—*the cervical factor* is today, for the figures reported for its incidence show great variation. To test this conjecture briefly we reviewed our last 50 cases of infertility with special attention to this factor. They were given a minute scrutiny for any evidence of even a minimal cervical or vaginal lesion. Such evidence was considered to be: visible cervicitis, cervical erosion, purulent or excessive cloudy cervical discharge, evident vaginitis, or the finding of vaginal parasites or fungi. According to these criteria, the incidence of *the cervical factor* in our small series of 50 cases was 70 per cent! As might be expected, other, sometimes more important, infertility factors were present in these patients (Page and Page,[6] studying patients from this area, found the average number of infertility factors per couple to be 2.4). But such a high incidence of cervical and vaginal lesions certainly cannot be by chance. We see nothing like it in the normal, fertile woman.

At the present time, however, even meticulous direct observation of the cervix and vagina probably will not always reveal the presence of *the cervical factor.* The Hühner Test, an immensely valuable diagnostic procedure, should never be omitted. Unfortunately, it has not been sufficiently employed and studied to bring its development to a satisfactory high point of neatness and accuracy. Its present technique is rough and gross. Aspiration or sampling of cervical mucus sometimes presents a problem in its dexterous, uncontaminated accomplishment. Methods for sampling from different levels of the cervical canal are only now in a process of development, and bid fair to provide significant findings. At present the interpretation of Hühner Test findings is not even well standardized—as is attested by disagreement between outstanding workers in the field.[8,15] Selection of the optimum time for the test, that of ovulation, is not rigidly adhered to so that the findings of many users are misleading. While it was originally felt that the test should be carried out within one to two hours after coitus, recent work suggests that more valuable information may be gained at four to six hours.

It is evident that the Hühner Test has not reached its full development. Its wider use, therefore, with refinement of its technique seems imperative; for it promises to give indispensable information about infertility factors. Many possibilities are open to those of us who will give this valuable investigative procedure its proper place in our armamentarium.

Along with our diversion of attention from *the cervical factor* our methods of treatment of cervical lesions have remained almost at a standstill. Indeed, in view of the delicate physiology of the cervix and the nicely balanced cervico-vaginal chemical relationships, one wonders whether some of our more vigorous therapeutic methods may not have left the patient more infertile than she was prior to their use. Too deep a cauterization may produce unfortunate cervical sequelae. Too extensive conization may remove too many of the essential mucus-secreting glands. Too vigorous chemical treatment may produce a chemical inflammatory reaction in the cervix which offers as much of a barrier to ascent of spermatozoa as did the original cervical lesion. We are just beginning to consider the use of our newer antibiotic and chemotherapeutic agents in the treatment of cervical and vaginal infections, and other, more delicate methods are only dimly envisioned. But unless we place proper emphasis on the importance of *the cervical factor* in infertility, the development of these methods will continue to lag.

We have all tended, in our desire to aid the oftenpitiful infertile couple, to grasp at straws in our attempts to elucidate the factors involved. The Rh factor is a case in point. Rh incompatibility has been called in question as a possible etiologic factor in infertility. Recent papers[1,5] have already shown rather convincingly that the previously-assumed role of the Rh factor in the causation of early abortion is mythical; it is even less likely that the similar assumption regarding its role in infertility is a valid one.

Rather than devote too much of our time to grasping at such straws let us return to a more searching study of familiar but poorly-understood infertility factors. Of these *the cervical factor* is perhaps the most deserving of our attention.

Discussion by PENDLETON TOMPKINS, M.D., *San Francisco*

I have been wondering in what respect the specialist in sterility possesses an advantage over the general practitioner. The difference is not in knowledge (for Dr. Overstreet has refreshed our recollection of the factors essential for reproduction), nor in equipment (for the specialist possesses no instruments not found in the office of the general practitioner excepting a curette for office endometrial biopsies and a machine for tubal insufflation). Even these two instruments may be temporarily dispensed with, for the basal temperature graph gives information regarding ovulation which is comparable to that provided by endometrial biopsy, and a uterosalpingogram is a substitute (though a poor substitute, in my opinion) for tubal insufflation. Since the specialist requires no rare knowledge and no indispensable equipment, what is the basis for his reputation? Simply this: thoroughness. He takes the time to secure a complete history, he procures blood counts, urinalyses, Wassermann tests, basal metabolism tests; he secures accurate temperature graphs and

records of coitus, and he insists upon complete sperm counts. Dr. Lewis Michelson of San Francisco, one of the eminent students of male fertility in this country, requires studies of three different specimens of semen before evaluating male fertility. He feels that a single specimen may be exceptionally good or exceptionally poor and quite unrepresentative of the normal of the individual.

The specialist in female infertility will scrutinize the cervix with a more critical eye than any other gynecologist. It does not suffice that there is no gross evidence of endocervicitis. The cervical mucus should be examined for leukocytes indicating cryptic endocervicitis. The canal should be delicately probed to discover pockets, synechiae or adhesions. These are important, not because they obstruct the passage of sperm, which are after all much smaller than a red blood cell, but because these pockets interfere with cervical drainage and are associated with abnormal cervical mucus. In every study the cervix should not only be gently probed and sounded but also should be slightly dilated. I have often wondered what part cervical dilatation has played in those cases of conception which have followed "the initial examination," an endometrial biopsy without other treatment, or a single tubal insufflation. In such cases the passage of an instrument through the canal may have been more beneficial than was recognized.

Endocrine therapy has been used in many forms and according to many schedules to stimulate ovulation or to increase the sperm count. If our present evaluations are correct the only certain effect of such therapy is to delude at least one person—the physician administering it.

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Surgical Operations Upon the Aged

J. Norton Nichols, M.D., *Los Angeles*

THE number of patients in the advanced age group increases with each passing year. We are told that 80 years ago, at the close of the war between the States, the average life expectancy of a baby was 40 years. Today it is 60, with the indications of a still further extension of the life span. There are in our country today approximately 10 million persons of an age of 65 or beyond, and the infant born this year, if he attains his 65th birthday, should find himself one of twenty million as old as he is or older. The care of this group enters the life of every physician, and this discussion pertains to the surgical aspect of that service.

What constitutes the "aged" patient? We have mentioned 65 as a working point, yet certainly age itself is not determined by the calendar. Circulatory deficiency, renal impairment, obesity, diabetes, and many other conditions may so alter the picture that an individual becomes older than his stated age. For clarity in this presentation it will be assumed that we are speaking of patients past 65 who are normal for age, or of those perhaps younger with unfavorable factors which bring them up to the same life expectancy. The term "surgical age" would be a good one and might well be used in each doctor's record showing his estimate of that patient as compared with an imaginary normal. Thus an individual of 60 might be tabulated as having a surgical age of 70, if in the opinion of his physician his condition was no better than the normal for the latter group. Such a classification might prove valuable in considering the advisability of elective surgical procedures.

The most common conditions contributing to a poorer-than-normal status are, in the order of this writer's prejudice, cardiovascular disease, obesity,

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renal insufficiency, diabetes and a senile or poor mental outlook.

Cardiovascular disease, because of its far-reaching secondary effects, must head any list of unfavorable factors in patients past middle age. Certain phases, such as congestive heart failure, cardiac asthma and emphysema, may create an almost prohibitive surgical risk. On the other hand, arteriosclerosis without symptoms, hypertension and coronary disease are not necessarily deterrents. It is rare to see a patient with a heart known to be poor, or one with damaged coronary arteries, act badly during or following an operation. Forewarned being forearmed, a skilled cardiologist is brought into the picture both pre- and postoperatively. With surgical trauma minimized as much as is humanly possible, the blood pressure carefully maintained at the preoperative level and with early ambulation, these patients do surprisingly well.

Obesity, in the opinion of the writer, is a commonly ignored yet most potent deterrent to a successful surgical result. Larger incisions, lengthened operating time with increased tissue trauma, anesthetic difficulties, poor wound healing, the inability of the patient to move himself postoperatively or to practice deep breathing, and the impracticability of early ambulation add up to a tremendous total in the mortality and morbidity tables. If a surgeon performs one hundred cholecystectomies in older patients with normal physique and 95 will live, and in a parallel group of grossly obese the recovery rate is 90 per cent, it would seem that there is but 5 per cent difference in the two series. But turn the figures around—five deaths in one group against ten in the other—and the mortality rate is seen to be twice as high. A longevity table prepared by Joslin from Bortz compares a group of nine obese individuals age 40 with nine of normal weight. At sixty the survivals are six against eight; at seventy, three against five; and at eighty, one compared to three. Since the cure of this malady can be effected through supervision and self-discipline, it does not seem amiss to suggest that elective operations in the grossly obese be declined or postponed. It is fair neither to the surgeon nor to the patient to assume an unnecessary risk.

Renal insufficiency is so closely linked with cardiovascular disease that it might well have been included in that classification. The occasional acute kidney failure with anuria is, however, so formidable a complication that it deserves special mention. Here prevention is far more valuable than cure. A careful history, combined with a nonprotein nitrogen value, a urea clearance test, a measured 24 hour output, and sometimes catheterization for residual urine, may avoid a fatality. Postoperatively the best guide is the excretion of at least 1000 cc. of urine per day with an acceptable specific gravity. If oral intake does not produce this, intravenous fluids are indicated. Those solutions made up with saline should be limited to 1000 cc. per day. Glucose in water may be used in any amount desired.

Diabetes if neglected can prove acutely dangerous, yet if it is controlled the operation can be made quite safe. In operating on a diabetic the surgical procedure can never be taken in stride. An internist skilled in the treatment of this disease can bring the patient to the operation timed almost to the minute and in perfect carbohydrate balance, and supervision by the internist should continue through every step of the postoperative period, especially when solutions of glucose are used. There are few occasions in surgery where so close a liaison of professional services is required.

A poor mental outlook is another unfavorable sign. It is very difficult to help a patient through a dangerous situation who has neither a spirit of cooperation nor the will to live. This attitude may be sensed in advance. It may be brought out by friendly conversation on other than medical subjects. Is he alert? Is he interested in current events? Has he a hobby and does he show a genuine interest in living? From such an interview one can form some estimate of the degree of brain cell degeneration. Certain it is that an elderly patient who is alert, cooperative and who really wants and expects to get well, will do far better than one who is depressed, disinterested or resigned —senile.

The advances made in the specialty of anesthesia have probably contributed more toward the safety of the aged surgical patient than has any other one factor. The old are never good anesthetic risks, and there is nothing more gratifying than to observe the skill with which the expert anesthetist handles his responsibility. All anesthetic agents are depressing and these patients should not be depressed. It is this writer's practice to choose only the best anesthetist, to acquaint him with the contemplated procedure and expect that he see the patient the night before operation. The choice of sedatives and anesthetic agents is then left in his hands. This ideal, however, cannot always be attained and where such is the case the usual routine is modified as follows.

All premedication is reduced. If a barbiturate is used the night before, it is limited to one capsule. The morning of operation, if the patient be small, very old or weak, it is again limited to a single capsule and the opiate is reduced to about one-half the usual dose. These drugs are administered far enough in advance so that their full effect is obtained before the anesthetic is begun. Induction of unconsciousness with pentothal or nembutal intravenously has become very popular and justly so, but the anesthetist must be watchful of the temporary repiratory depression, and be prepared to combat it if it persists too long. An airway, a laryngoscope and an oxygen tank are "musts" in the equipment within reach.

So many combinations of anesthesia are now available that it would be cumbersome to attempt to discuss them. Bare unconsciousness with pentothal plus local infiltration may be indicated at times. A preference is admitted for spinal instead of general anesthesia in most cases. By keeping the spinal dose small and again using pentothal sparingly, muscular relaxation is obtained with the patient lightly asleep. For leg amputations a hemispinal is perfectly feasible. In this, with the patient lying on the affected

side, a small amount of a heavy solution is injected. This sinks against the nerve roots on the dependent side and anesthetizes that leg only. Spinal anesthesia seems to present but little hazard to the aged patient provided the dose be small, the level of the anesthesia be kept below the intercostals, and the blood pressure held at the pre-anesthetic level with ephedrine. General anesthesia by inhalation, however, has been our standby for years and meets with no objection from the writer if muscular relaxation can be obtained without carrying it to a deep level. This is often difficult to accomplish.

In operating room preparation all efforts possible should be made to avoid the loss of body heat. Old people feel the cold, and are depressed by it. All skin disinfectants evaporate quickly and chill the surface. An avoidance of overexposure plus warm blankets over the covered parts should be the rule.

As to operative technique, every refinement of gentleness and hemostasis at the surgeon's command should be used on aged patients. Speed is no object if attained through rough handling. The older the patient, the greater the liability to shock, and this is usually brought about by tissue trauma and blood loss. Patients with thickened blood vessels actually have a diminished blood volume so that any loss becomes proportionately greater. No one single item adds so much to the safety factor as does a blood or plasma transfusion running during the operation. This is far more advantageous than its administration before or after. Non-elastic blood vessels do not take kindly to sudden rises and falls of pressure, and shock once developed is hard to combat.

Old tissues heal more slowly than normal. The abdominal closure is therefore subject to two demands, namely, that the wound edges be safely held as long as is necessary, and that the closure be of sufficient strength to allow early ambulation. Silk and cotton meet these qualifications, and cat-gut will also if it is reinforced by many retention sutures of non-absorbable material. An instructive observation came from a study of wound ruptures in the largest hospital in Los Angeles. In every case of disruption retention sutures had been used, but in no case more than three.

The aim of postoperative treatment should be toward prevention of those complications most likely to occur. They are pulmonary, renal, and circulatory. Oxygen, either by tent or mask with frequent CO_2 ventilation is a valuable safeguard against the first and last of these. Saturation of the blood with oxygen aids the heart in its task of increased oxidation. Frequent turning of the patient is advisable but may be overlooked unless specifically ordered. Morphine is just as valuable as it is in younger patients, although the dose should be smaller. Barbiturates are used sparingly if at all, because of their tendency to confuse and depress.

The kidney function in old people is notoriously poor. Intake and output should be charted, and the latter not allowed to fall below 1000 cc. per day; 1500 cc. were better. If output is below 1000 cc. a day intravenous fluids must be increased. Five to ten percent glucose solution in water seems to work best. Frequent voiding of small amounts calls for catheterization for residual urine. In wasting diseases where hypo-proteinemia can be assumed or proven, amigen is of extreme value. Vitamins, especially C, are used routinely to favor wound healing.

Early ambulation has recently been the subject of much favorable discussion. Whatever its merits may be, they are magnified in the aged. Nothing is more conducive to a return of morale. Bowels and kidneys act more promptly, gaseous distension and catheterization are minimized, appetite returns more quickly and a more hopeful attitude is apparent. From all reports, wound disruption is not increased by early ambulation. This last may be true, but because of the responsibility the surgeon assumes in departing from a conservative precedent, this writer suggests that incisions be sutured with an eye to additional security if early rising is contemplated.

Age itself is no barrier to surgery. The writer is fully aware that this paper offers nothing new. It will have served its purpose if it reminds us afresh that in no other class of patients do careful precautions and attention to detail mean so much. Life is often just as precious to its owner at 70 as it is at 30, and because of his diminished sphere of living pain becomes even more intolerable. Surgical risk is greater—just how much may be hard to determine. We are told that ordinary surgical mortality becomes doubled at 50, trebled at 60 and quadrupled at 70. This affords an opportunity to consider elective operations from a statistical or mathematical angle.

Nothing is more uncertain than one life; nothing surer than the law of averages on a million lives. The tables of life expectancy used by insurance companies are highly accurate when applied to a group. At 50 and normal for age, a man's life expectancy is 20 years or to age 70. For each year that he has lived beyond 50, one-half year is added to 70. Thus at 60 his expectancy would be to 75, at 70 to 80, and at 80 to 85. In the older brackets it may sometimes be well, therefore, to think of life not as an abstract whole, but rather as a definite sum of year units. Surgical measures with their attendant dangers and chances of failure then help form an imaginary equation. If the reward for success (a full life expectancy) is not greater than the surgical risk plus the patient's expectancy under palliation (which is forfeited when operation is performed) then perhaps the more radical course should be abandoned.

No part of this discussion pertains to the necessary emergency operation, no matter what the odds may be. Nor does it apply to operations for those in constant pain. These patients are entitled to any choice they may wish in seeking relief, for although life may be estimated in units of years, living is measured in terms of comfort. Outside of these, however, there will always remain a group of elective conditions in which surgical operation may offer something more or take everything away. It is toward these cases that the mathematical angle may help point the way in estimating expected gain against possible loss.

1930 Wilshire Boulevard.

The Present Status of Female Sterilization Techniques in the United States

Robert J. McNeil, M.D., and A. N. Webb, M.D., *Los Angeles*

THIS study was undertaken to discern the methods of sterilization used by leading gynecologists and obstetricians in their own practices. Although there are many carefully prepared and critically analyzed reviews of tubal sterilization techniques presented at regular intervals in the literature, each of these studies is presented to extol the virtues of one technique. To crystalize the opinions from the various sections of the United States, we have sent a questionnaire to the members of the teaching staffs of the medical centers and in this paper we have summarized the returned answers.

Historically, sterilization of the female has been of interest to the medical profession since first contemplated by Hippocrates as a means of eliminating hereditary perpetuation of the insane. It is difficult to trace accurately the earliest attempts at sterilization because we have reports of cesarean sections in Sanskrit translations on ancient Hindu medicine from the fifth century. There are Biblical references to cesarean operations in Jewish history from the second cenutry.[4] It is not illogical to assume some attempts at sterilization were made in the early centuries.

In the early part of the Nineteenth Century, G. P. Michealis suggested hysterectomy with cesarean section for sterilization, and in 1834 von Blundell removed the uteri from four rabbits. Of the four rabbits hysterectomized, three lived, giving reassurance to those who were to attempt gynecological surgery in the years following. His technique included bringing the stump of the cervix to the abdominal wall, a forerunner of Porro's operation, introduced in 1877. Von Blundell is also credited with the initial written suggestion of tubal sterilization in his textbook, published in 1834. The method he suggested was tubal resection, but he wrote that simple division might successfully prevent pregnancy.

Froriep, in 1850, suggested the creation of a chemical slough stricture in the upper uterine angles to prevent pregnancy. This was the forerunner of the recent suggestions for sterilization by intrauterine cauterization. During this era, the uterus was thought to have definite endocrinal function, so hysterectomy was rarely done for primary sterilization. In 1880, Lungren of Toledo, Ohio, tied both tubes after a second cesarean operation; this is the first recorded truly tubal sterilization. It is of interest to observe that that his follow-up notes elaborated upon the regular monthly menstruation after the operation, indicating the paucity of knowledge about the physiology of menstruation at that time.

Read before the Section on Obstetrics and Gynecology at the 76th Annual Session of the California Medical Association, Los Angeles, April 30, 1947.

Between 1880 and 1910, a wide variety of procedures were carried out with uniformly poor results. A report by Leonard[8] in 1913 emphasized the high incidence of failure in all methods of sterilization, including cornual resection, intra-uterine cauterization, and total salpingectomy. Nurnberger's report in 1919 described 36 methods of tubal sterilization and concluded that salpingectomy or cornual resection was the best. The large number of procedures in his report emphasizes the keen interest in perfecting a reliable technique.

Madlener's publication in 1919 received widespread acclamation in this country and in Germany. The certainty of the results, however, were questioned as early as 1921 by J. Whitridge Williams,[13] although in 1926 and again in 1932 Madlener published two series without known failure..

Many new techniques were developed from 1920 to 1940. Unusual among the procedures suggested for sterilization was intra-uterine actual cautery to the tubal openings, propounded as a "simple office procedure,"[1] and the creation of a double vagina, one to be a blind pouch for coitus, and the other for pregnancy.[5]

Von Groff[10] reviewed 4,279 cases of sterilization by the Madlener technique, wherein he made critical analysis of the failures. He attributed them to slipping of the ligature, laceration of the serosa which encouraged fistula formation, and tying of the round ligaments by error. He concluded that the failures resulted from not adhering to Madlener's exact technique.

Dippel[2] in 1940 studied postoperative tubal specimens with serial microscopic sections from five patients who became pregnant after sterilization by Madlener's method. He reemphasized von Groff's findings on the technical failures, and demonstrated two cases of endosalpingiosis, a process which Sampson publicized in 1921.

Lazard,[7] in 1940, reviewed the entire subject and concluded that subtotal hysterectomy was the most satisfactory procedure.

In 1933 and again in 1939, Lull[9] reported extensively upon the method of tubal sterilization introduced by Pomeroy, stating that in his clinic the method had given exceptionally fine results. His careful analysis of the reported failures of the Pomeroy method bears out the importance of exactly adhering to the technique. His papers offer proof that Pomeroy's technique is the simplest and safest of the tubal type sterilizations.

In 1946, Knight[6] compared the results of the Pomeroy operation with the published statistics on the Madlener method. He concluded that the 0.31

per cent failure in the Pomeroy operation was better than the 0.6 per cent average of failures in a large series of the Madlener type.

Any discussion of sterilization procedures cannot circumvent the problem of endocrinal failure attendant to the operation for sterilization, and for that reason a brief review of the literature is presented. Lungren's contribution that tubal ligation did not interfere with menstruation has been mentioned. Dippel,[3] in 1939, demonstrated that only 16.6 per cent of patients had menopausal symptoms following hysterectomy, when sterilization was the primary indication for surgical operation, but that more than 67 per cent of the patients who had a hysterectomy for definite pelvic disease complained later of menopausal symptoms. He concluded that involvement of the ovaries in the disease, rather than the hysterectomy itself, was the principal cause of endocrine failure.

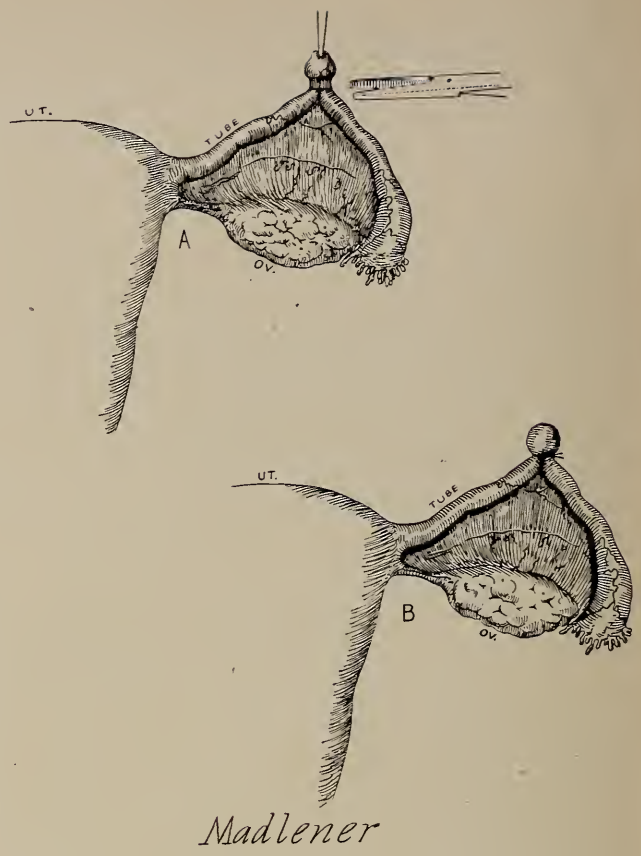
Vruwink[11] and Papenoe undertook an exhaustive study of libido following sterilization in 1930 and concluded that one woman in four does not enjoy coitus after sterilization, but that this fact is not mentioned to the surgeon, usually because he does not ask about it. They also concluded that bilateral salpingectomy did not affect libido; in fact, one third of the patients reported improved sex life when pregnancy was no longer feared. Hysterectomy, plus salpingectomy, had no demonstrable effect on libido, according to their records. It is of interest to discover in their conclusions that bilateral oophorectomy may leave the well adjusted woman with no change in her satisfactory sex life, but that the young, unadjusted and near menopausal woman is usually quite dramatically affected; her libido is markedly decreased. Watson[12] concluded that the removal of the uterus does not tend toward earlier menopause.

After careful perusal of the available history of sterilization which has been presented here in condensed form, it is concluded that the following five methods of tubal sterilization have apparently survived the test of time and are in common use. These were the basis for our questionnaire and the methods seem to serve most obstetricians and gynecologists in the United States. Many indicated that they used variations of several of these methods and only one or two used a new technique.

1. Madlener sterilization which consists of bringing up the fallopian tube through a small abdominal, or posterior coloptomy incision, crushing its middle third and tying the loop with non-absorbable suture. (See illustration).

2. The Pomeroy technique (see illustration) which resembles the Madlener operation, in that it can be done through the small abdominal or posterior coloptomy incision. The tube is grasped in its mobile middle third and pulled up to a loop, which is tied with fine absorbable catgut. There is no preliminary crushing of the tube. The loop lying above the tie is then excised and after a very careful check for bleeding, the tube is dropped back.

3. The cornual resection (illustrated) which consists of the excising of the cornual portion of the tube in a wedge shape. The margins of the incision are carefully closed and the bleeding arrested. The remaining cut end of the tube is buried into the broad ligament and the raw areas covered with the round ligament.



Madlener

4. The method devised by F. C. Irving. He divided the tube in its middle third and buried the cut end of the proximal portion into the myometrium of the posterior corpus. (See illustration).

5. The Watson method of tubal sterilization which consists of excising the middle portion of the tube and burying the proximal cut end into the broad ligament, as shown in accompanying illustration. The distal cut end lies free in the abdomen.

Upon the background of the historical and literary review of the sterilization problem, we present the results of the questionnaire sent to leading members of the American Board of Obstetrics and Gynecology in each section of the country. A distinct effort was made to send queries to men closely affiliated with medical teaching centers. Table 1 is a replica of the questionnaire answered by 124 of these men.

We received replies from more than 70 per cent of the doctors. Many of the remaining questionnaires were returned unanswered because of war displacement.

The returned questionnaires have been analyzed in several ways in an attempt to show: (1) Which procedure for sterilization is the most universally used by obstetricians and gynecologists. (2) What change in procedure is made when sterilization follows cesarean section or is a part of laparotomy; (3)

TABLE 1.—*The Questionnaire Which Supplied the Data for This Study.*

Which of the following methods do you employ as a usual routine in sterilization?

	Following Cesarean	With Laparotomy
a. Pomeroy		
b. Madlener		
c. Cornual resection		
d. Watson		
e. Subtotal hysterectomy		
f. Other		

What percentage of cases do you *estimate* show menopause symptoms one to three years after hysterectomy when that operation has been performed on women under 30 years of age?.....%.

Regional influence from adjacent medical centers upon procedures chosen; (4) The impressions of obstetricians and gynecologists concerning the onset of menopausal symptoms following hysterectomy in women under 30 years of age.

It was difficult to decide what definition could logically be applied to the regions selected. The influence of medical schools and prominent authorities in geographically adjacent areas intermingled and divided opinions most profoundly, especially in the areas between New York and Washington, D. C., and in the Chicago area. However, the areas selected as units comprise the results from cities as listed; the inequalities and ambiguities of our regional divisions are recognized but the results do bear contemplation. Table 2 lists the cities included in each area.



Table 2.—*Cities in the Various Areas to Which Questionnaires Were Sent*

Los Angeles Area:	South:	Chicago Area:	Northwest Area:
Santa Monica	Huntington, W. Va.	Indianapolis	Portland
Beverly Hills	Birmingham, Ala.	Rochester. Minn.	Vancouver
Glendale	Washington, D. C.	Milwaukee, Wis.	Seattle
Pasadena	New Orleans	Detroit	New England Area:
Los Angeles	Morehead, N. C.	Cleveland	Providence
San Diego	Charlottsville, Va.	Chicago	Manchester, Conn.
New York Area:	Durham, N. C.	St. Louis	New Haven, Conn.
Syracuse	Nashville, Tenn.	Columbus	Boston
New York	Charlotte, N. C.	San Francisco Area:	Midwest Area:
Englewood, N. J.	Louisville, Ky.	San Francisco	Omaha
Brooklyn	Spartansburg, S. C.	Sacramento	Oklahoma City
Jersey City	Atlanta, Ga.	Berkeley	Kansas City
Atlantic City	Augusta, Ga.	Philadelphia Area:	Iowa City
Rochester, N. Y.	Little Rock	Philadelphia	Denver
Baltimore	Miami, Fla.	Pittsburgh	San Antonio



Cornual

The sectional influence can be graphically emphasized. Table 3 shows the sterilization procedures chosen with cesarean section. Herein is indicated the distinct preference for the Pomeroy technique in the area surrounding New York, Philadelphia, and in the South. In and about Chicago there is a slight favoritism for Madlener's method. However, the Los Angeles regional survey demonstrates an inclination toward subtotal hysterectomy not reported from other parts of the United States. Preferences from other areas varied, but it is apparent that most of the physicians who answered use either Pomeroy, Madlener, or cornual resection techniques routinely.

TABLE 3.—*Method of Sterilization Used in Various Areas in This Country*
(Cesarean)

Area	Pomeroy	Madlener	Irving	Cornual	Watson	Hysterectomy Subtotal	Hysterectomy Total
Los Angeles	4	1	0	2	1	4	0
New York	17	4	0	1	1	0	0
Chicago	7	10	1	8	2	1	0
San Francisco	2	2	0	2	1	0	0
Philadelphia	7	3	0	0	0	0	0
South	11	2	1	6	0	0	0
Northwest	1	0	0	3	1	0	0
New England	2	1	2	0	0	1	0
Midwest	5	4	0	1	0	0	0
Total	56	27	4	23	6	6	0

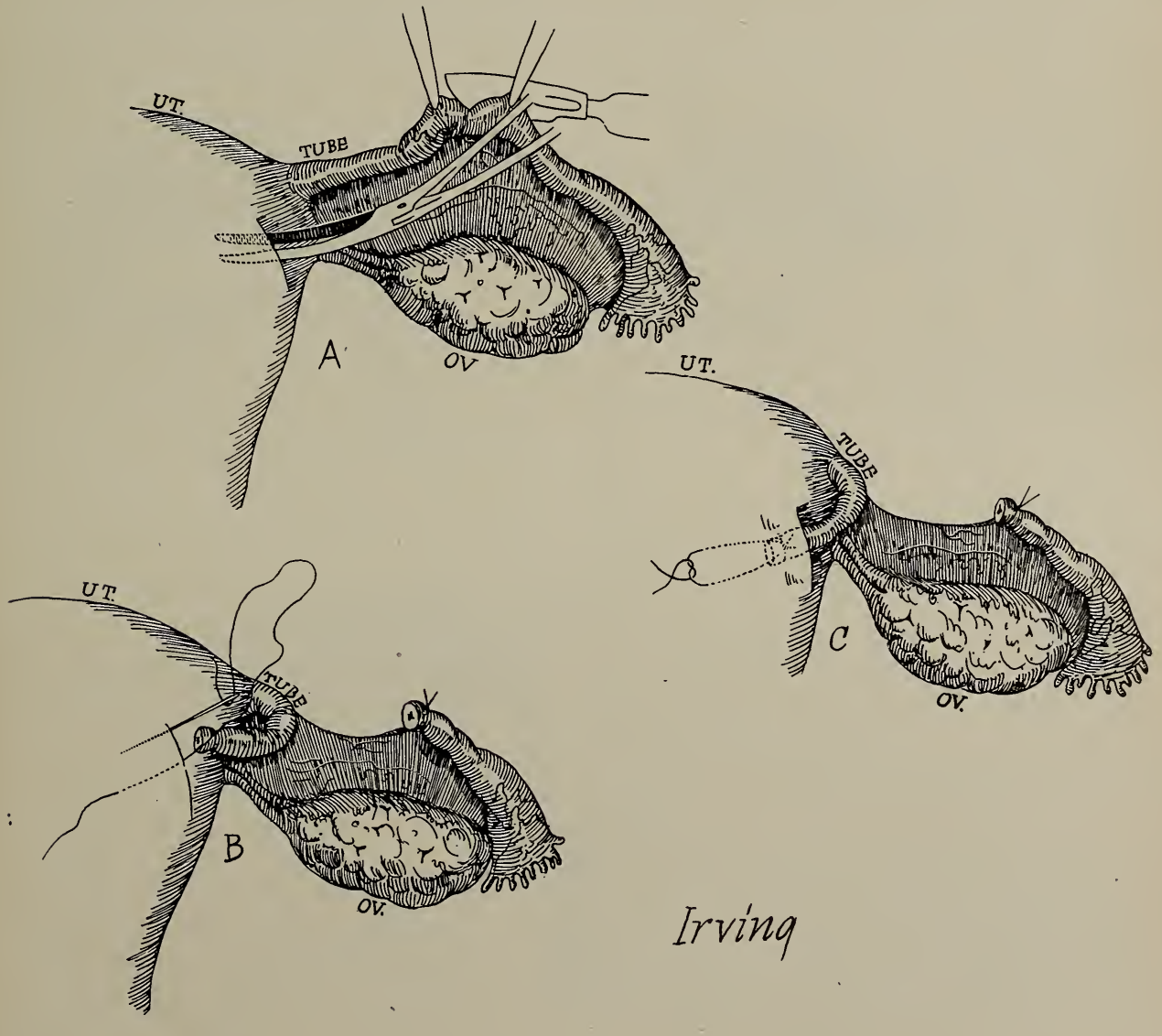
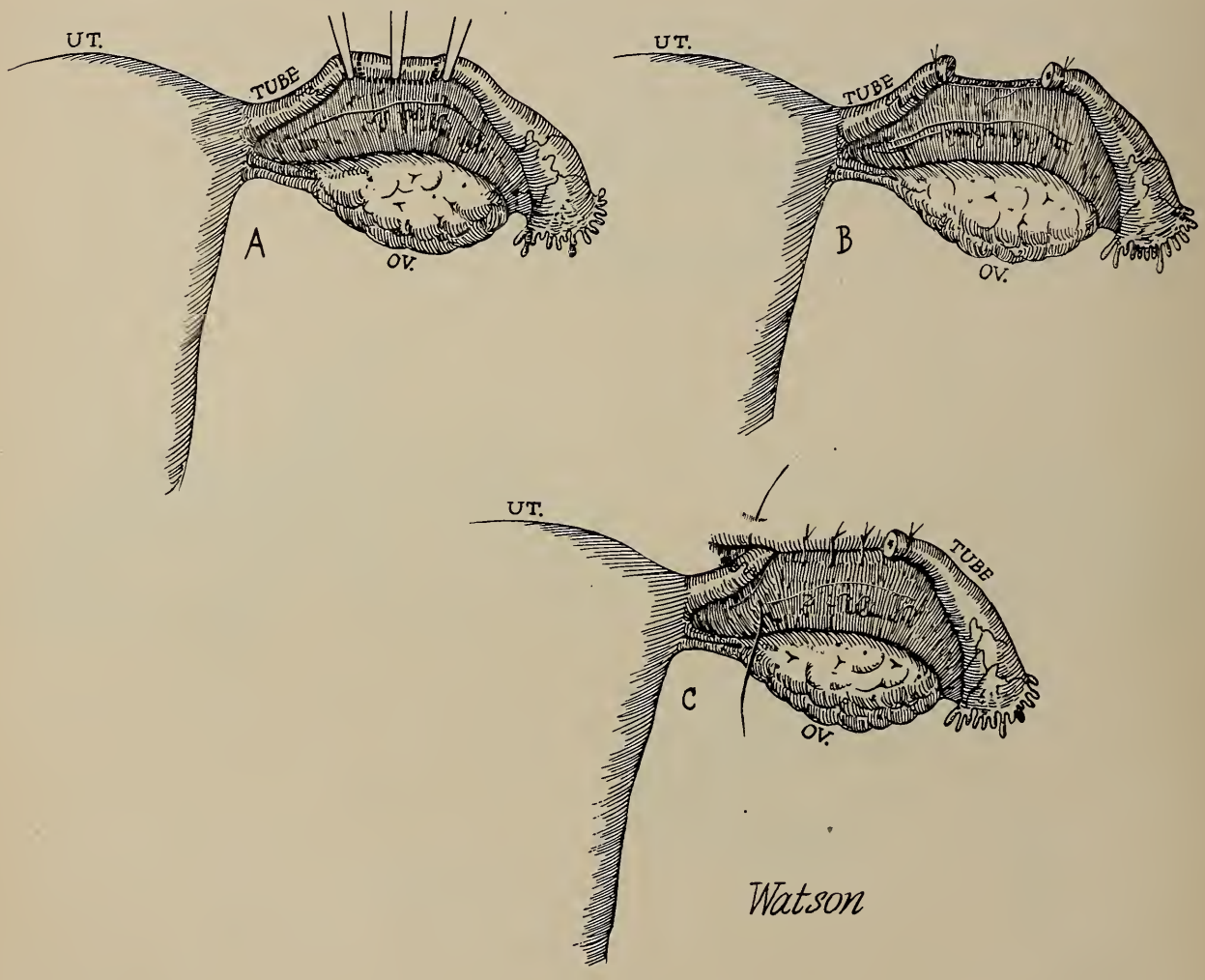


Table 4 shows the methods of sterilization used when laparotomy is done. In most instances these sterilization procedures were stated to be postpartum sterilizations. Many replies distinctly differentiated a change in technique to hysterectomy in cases in which there was a history of functional bleeding or any disease in the uterus or adnexa. Keeping in mind sterilization as the primary indication for operation, we can present the following observations. The New York area again prefers the Pomeroy method as a routine, but with increasing preference for cornual resection. The Chicago region indicated a shift toward cornual resection as the procedure of choice. There is no change of consequence in the figures from the South, except that two who answered from that area prefer total hysterectomy exclusively; this choice is also indicated in one reply from New England. Other sections of the country appear to be about equally divided in the choice of Pomeroy, Madlener and cornual resection with the exception of the Los Angeles area where subtotal hysterectomy again takes a prominent lead.

TABLE 4.—*Methods of Sterilization Used in Various Areas of This Country*
(Laparotomy)

Area	Pomeroy	Madlener	Irving	Cornual	Watson	Hysterectomy Subtotal	Hysterectomy Total	Salpingectomy
Los Angeles	2	0	0	2	1	6	0	0
New York	13	3	0	6	1	0	0	0
Chicago	6	7	1	10	2	1	0	0
San Francisco	0	2	0	2	1	0	0	0
Philadelphia	5	3	0	0	0	0	0	0
South	10	1	1	7	0	0	2	0
Northwest	0	0	0	3	1	0	0	0
New England	0	0	2	2	1	0	1	1
Midwest	3	4	0	2	0	0	0	0
Total	39	20	4	34	7	7	3	1



Again we repeat, many answers included comments to the effect that a hysterectomy, total or subtotal, was done if there was uterine disease; the choice of operation depended upon the indications dictated by existing conditions. These figures presented do not include hysterectomies as a sterilization procedure, unless the reply to the questionnaire indicated that sterilization was the primary reason for removing the uterus.

Many of the doctors included comments with the questionnaire. Among the most frequent of these was that cornual resection had been the procedure of choice until recently, usually about 1941, but that Pomeroy's technique is now replacing it because there is less bleeding and it is simpler and quicker.

In summary then, on this phase of our presentation, from 124 replies we found the results shown in Table 5. The Pomeroy technique is the most frequently used following both cesarean and laparotomy. Madlener's method is next most frequently used with cesarean, but the cornual resection is used more often with laparotomy.

TABLE 5.—*Methods of Sterilization in the Order of Frequency of Use with Cesarean Section and Laparotomy.*

	Cesarean	Laparotomy
Pomeroy	56	39
Madlener	27	20
Cornual	23	34
Watson	6	7
Subtotal Hysterectomy	6	7
Total Hysterectomy	0	
Irving	4	4
Salpingectomy	0	1

The answers to the question on the incidence of menopause symptoms within three to five years following hysterectomy in women under 30 years of age were interesting because of the diversity of opinion. Ninety-seven of the physicians returned a reply to this question, but 14 either (a) had not heard of the problem; (b) had insufficient experience to warrant an opinion; or (c) did not do hysterectomies on women under 30 years of age.

Experience among the remainder of the doctors ranged from 0 per cent to 98 per cent. It is quite apparent from Table 6 that the majority felt that there were no menopausal symptoms from the hysterectomy per se. However, five physicians thought that 95 per cent developed symptoms. To analyse a little further, 18 of the answers indicated such symptoms were present in more than 50 per cent of the patients, but 32 felt that they were present in none, and 44 replied that they were present in 1 per cent or less. One physician stated that menopausal symptoms followed cesarean section hysterectomy in only 15 per cent of the total number of cases, but that 40 per cent of the non-pregnant women developed the symptoms following hysterectomy.

TABLE 6.—*Percentage of Patients Under 30 Years of Age Showing Menopausal Symptoms After Hysterectomy.*

Answers to Questionnaire		
No opinion	14	
0	32	44
1	12	
5%	5	
10%	6	
15%	4	
20%	5	
25%	1	
50%	6	18
75%	4	
90%	3	
95% and over	5	

Many parenthetically injected comments brought out the thought that hysterectomy is seldom done in the absence of disease. The disease which involved the tubes and ovaries caused the development of the menopausal symptoms rather than did the hysterectomy itself.

In conclusion, we recapitulate the results of our questionnaire to show:

1. The Pomeroy method of tubal sterilization is the most frequently used following cesarean section and with laparotomy.

2. The Madlener technique is the second most popular method used after cesarean.

3. Cornual resection is the second most popular method with laparotomy.

4. Hysterectomy is chosen when uterine disease exists.

5. A majority of the physicians who answered our questionnaire believe that less than 1 per cent of the women under 30 who have had a hysterectomy suffered menopausal symptoms within three to five years.

103 South Ardmore Street.

The authors are indebted to 124 physicians who showed the interest and courtesy to answer our questionnaire. The interest of Dr. Clifford Lull, who replied at length and sent reprints of his work is especially appreciated, and we are grateful also to the many who wrote their personal comments to help us evaluate their opinions.

Discussion by DONALD G. TOLLEFSON, M.D., *Los Angeles*

I am particularly interested in discussing sterilization from the medico-legal standpoint, for it must be constantly emphasized that the proper consent must be obtained from both the patient and her husband. This authorization blank should state that both the parties understand that the operation *may* render the individual sterile. This must be signed in the presence of a witness and the patient must not have had sedation within a reasonable length of time before the signing which might render her incapable of making the decision. It is also advisable to explain to the patient and her husband that the procedure cannot be undone once it has been performed. In the event that a laparotomy for pelvic disease may render the patient sterile, the couple should be informed of this possibility.

Sterilization without indication carries a real hazard to the physician from a legal standpoint, for, according to law, only the mentally ill patients committed to an institution may be so treated. While the consent of both husband and wife to an operation they have been told might make the wife sterile might seem sufficient (and no cases in this state have been tried), it is almost certain that sooner or later a physician may be called upon to explain why the operation was done.

It would, therefore, seem advisable that consultation with another physician be had whenever this procedure is considered.

It also should be brought out that the surgeon who performs the operation is responsible for his act and therefore ought not be just a technician. He must be able to justify his action with full knowledge of the facts, and not depend upon a referring physician to bear the responsibility. This is true for sterilization in either male or female.

Elective sterilization should not be treated too lightly, and some indication with a consultation of other physicians should be the rule.

This paper is interesting from several standpoints. It covers the history of sterilization techniques. It also reveals the wide variation in methods used in different medical centers of the country. The method chosen is apparently popular because of the stimulation of local outstanding physicians rather than its relative value over other types of procedure. Another point of interest is the evident marked difference of opinion among leading gynecologists as to what constitutes menopausal symptoms.

I should like to discuss the practical application of a few of the methods of sterilization mentioned. In 1938 I became acquainted with Robert Kimbrough in Philadelphia. He was using the Lull-Pomeroy technique at that time and had had a series of two hundred cases without a failure. I was struck with the simplicity of the procedure in comparison with cornual resection, especially at the time of cesarean section. To stop the venous bleeding from the broad ligments in doing cornual resection not infrequently took longer than the cesarean section. Since that time I have used the Lull-Pomeroy technique exclusively. It is not only an excellent means of sterilization with cesarean but it is also well adapted to the vaginal approach and the small, early post-partum, abdominal incision.

I am not an advocate of sterilization by hysterectomy in young women. An occasional failure or the rare development of a case of functional bleeding, following partial tubal resection is still on the whole preferable to the psychogenic or actual menopausal symptoms following subtotal hysterectomy. The wide variation in the percentage of menopausal symptoms following hysterectomy reported in the paper only indicates the difficulty in evaluating the importance and severity of such symptoms. I firmly believe that the patient should be given the benefit of the doubt and the menstrual function maintained whenever possible in women under the age of 36.

In cases where hysterectomy and sterilization are medically and legally indicated there is a place for fundectomy. The wedge-shaped excision of the fundus including the interstitial portion of each tube, allows the removal of the uterine contents and tubal interruption through one incision in the uterus. The soft tissue allows good peritonization.

In women approaching 40, I believe subtotal hysterectomy following cesarean section is the method of choice for sterilization purposes. Morbidity is less than with cesarean section and tubal ligation, the convalescence is shorter and the result more positive.

I have reviewed 27 cesarean hysterectomies performed during the past three years. The follow-up records reveal very satisfactory results on the whole. Nine of the patients menstruate for one day. All but one of these nine have stated that they wish I had stopped the process entirely. The other 17 have no different symptoms than the ones who menstruate.

In conclusion, I believe that the reported results of the Lull-Pomeroy technique of sterilization warrant its continued use in preference to subtotal hysterectomy in women under the age of 36. Fundectomy is the operation of choice in cases requiring hysterotomy and sterilization. Beyond the age of 36 the uterus can be removed at the time of cesarean as a means of sterilization with good results.

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The Diagnosis of Scleroma

Orlyn B. Pratt, M.D., Milton G. Levine, Ph.D., and
Robert E. Hoyt, Ph.D., *Los Angeles*

RHINOSCLEROMA was first described in 1870 by von Hebra.[14] He considered it an unusual form of skin cancer. Geber[3] recognized the lesion as a chronic inflammatory process accompanied by perivascular cellular infiltration and connective tissue proliferation. Mikulicz[9] described the histological picture which is now recognized as being characteristic of the disease. The "foam" or "lace" cells seen in this granuloma bear his name.

As the disease is not confined to the nose as von Hebra originally assumed in using the prefix "rhino," the more inclusive term "scleroma" was officially adopted at the Second International Congress of Otorhinolaryngology[11] held in Madrid in 1932.

INCIDENCE

Scleroma was once thought to be confined to Central and Southeastern Europe, but it is now recognized more often and is generally acknowledged as world-wide in occurrence. In a comprehensive report, Cunning and Guerry[1] in 1942 reported that 102 cases had been described to that date in the American and Canadian literature. Streit[13] contends that an endemic area exists in Central Europe, especially Poland. Lasagna[6] feels that it is becoming more common in Italy, and there is some evidence that the disease is seen frequently in Central and South America.

PATHOLOGY

Scleroma is a chronic disease of the upper air passages involving the mucosa and submucosa. Clinically, three stages are described. The first stage resembles atrophic rhinitis with profuse secretion, crust formation and foul smell. The second stage is characterized by proliferation of tissue which leads to obstruction of the air passages. In the third stage there is cicatrization and stenosis causing marked deformity. The lesion usually starts at the anterior portion of the nostril in the mucosa. It may extend anteriorly and involve the skin in the vestibule and around the aperture of the nares. The lesion also progresses posteriorly involving the turbinates, pharynx, soft palate, uvula, pillars, larynx and trachea.

This disease is apparently transmitted by long contact under poor hygienic environment. No facts are available regarding the incubation period. The onset is insidious and the duration may be from 20 to 30 years. There is little effect on the general health except for the mechanical obstruction of the air passages which in extreme cases may lead to death by asphyxia.

The lesions may be classified in three types which roughly parallel the three clinical stages. In the earliest lesions gross examination shows atrophy of the mucosa with crust formation. Ulceration may result from trauma due to the atrophic epithelial covering. The microscopic appearance of the early lesions is not sufficiently characteristic to lead to a diagnosis of scleroma. In areas normally covered with stratified squamous epithelium there is atrophy of the middle layers (stratum lucidum and stratum granulosum) and disappearance of rete pegs, although there may remain an occasional irregularly shaped hypertrophied rete peg. The epithelial covering is thinned to two or three cell layers in thickness. There is regular arrangement of the basal layer of epithelial cells. In areas normally covered by ciliated columnar epithelium there is a multiplication of cell layers forming ciliated stratified columnar epithelium which later by metaplasia becomes atrophic stratified squamous. Covering the epithelial surface there is a crust formed of dried mucus and necrotic exudate. The pictures in the corium and submucosa are similar. There may be a narrow zone immediately beneath the epithelium which is comparatively free of inflammatory changes. Beneath this there is a granuloma of non-specific nature. The fibroblasts and capillaries are masked by the dense infiltration with wandering cells. The exudate consists chiefly of plasma cells but there are also lymphocytes, polymorphonuclears, mononuclears and histiocytes. Mikulicz cells are not present in sufficient numbers to attract attention.

The proliferative phase is not sharply defined from the atrophic. Nodules varying from 1 to 10 mm. in diameter occur singly or in groups. These, when first developed, are soft, later become hard. This tissue may completely fill the nasal passage from the nostril to the nasopharynx. When the larynx or trachea is involved, the proliferative lesion may lead to asphyxia. The facial appearance is sometimes markedly disfigured by the nodular lesions protruding from and surrounding the nasal orifice. The microscopic appearance at this stage is that of a chronic granuloma. The surface may be covered by atrophic stratified squamous epithelium without rete pegs or with a few hypertrophied distorted rete pegs. Part of the surface may be ulcerated and covered by a crust of necrotic exudate. The submucosa is replaced by a thin zone of collagenous tissue and granulation tissue composed of young blood vessels and fibroblasts. Beneath this zone the granulation tissue is filled with a dense infiltrate of plasma cells,

From the Institute of Experimental Medicine, College of Medical Evangelists, Los Angeles, California.

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lymphocytes and mononuclear cells. Colloid or hyaline cells with deeply acidophilic cytoplasma and small, darkly stained, eccentric nuclei and also a few Russell fuchsin bodies may be seen scattered throughout the granuloma. The cell most characteristic of this lesion is the Mikulicz cell. However, it may be found at times in granulomas of other types also. This cell is 15 to 20 times the size of a red cell, has a large clear vacuole and a small eccentrically placed nucleus on the cell membrane. Such cells may be scattered throughout the granuloma or they may occur in large groups forming foamy appearing, light staining areas. Frisch bacilli may be found in the vacuoles or in interstitial spaces around these cells. Collagenous connective tissue usually separates the granuloma from the underlying cartilage or bone.

In the stage of cicatrization there is marked distortion of involved structures. The tissue consists of hard, tough scar. Microscopically the section shows a disorderly array of heavy collagenous fibers with relatively few connective tissue nuclei. Here and there one may find irregular areas darkened by aggregations of pyknotic nuclei. A few atrophic gland acini are seen scattered through this scar tissue. An occasional island of granulation tissue or group of Mikulicz cells may be found. Bacteria are difficult to demonstrate in the section during this stage but can be recovered in cultures. The histological picture of this final stage of scleroma is not sufficiently characteristic to lead to a diagnosis without supporting evidence.

BACTERIOLOGY

We consider *Klebsiella rhinoscleromatis* to be the cause of scleroma. The organism was described by Frisch in 1882, and was asserted by him to be the causative agent. It is a short, plump Gram-negative bacillus, growing readily on ordinary culture media, where it forms mucoid, spreading colonies 2 to 5 mm. in diameter which become confluent when crowded. Fermentation of carbohydrates is characteristic: dextrose, maltose and mannite are fermented without production of gas. Lactose is not fermented, while sucrose is attacked slowly by some strains. Indole is not formed.

The reluctance of many workers to accept the bacillus of von Frisch as the causative agent is due in part to the failure to reproduce the disease in the experimental animal, and to the alleged appearance of the bacterium in the respiratory passages of healthy persons. In a study reported elsewhere[7] we found that *K. rhinoscleromatis* did not appear in the respiratory tract in 267 individuals. The Friedlander's bacillus *(K. pneumonia)* may be mistaken for *K. rhinoscleromatis* upon superficial examination, but the carbohydrate fermentation pattern distinguishes these two forms readily. *K. pneumonia* regularly ferments lactose and sucrose, and most strains produce gas in addition to acid.

A satisfactory procedure for the isolation of *K. rhinoscleromatis* from the respiratory tract of a suspected case is as follows:

Culture material from nose and throat are streaked heavily or smeared on eosin methylene blue plates. This inhibits the growth of Gram-positive microorganisms and favors the growth of the Gram-negative group. Plates are observed after 24 and 48 hours' incubation. Translucent mucoid colonies are subcultured again on E.M.B. streak plates, and isolated colonies are picked to agar slants. When microscopic examination indicates the culture to be pure, carbohydrate broth tubes are inoculated. Readings are made at 24 and 48 hours. Strains fermenting dextrose, maltose and mannite with acid only and showing no reaction on lactose or sucrose are considered to be *K. rhinoscleromatis.*

These observations agree with those of Figi and Thompson,[2] and of Morris and Julianelle,[10] as well as with the less detailed reports of Gonsiorowski and Meisel.[5]

A possible source of confusion lies in the difficulty in obtaining pure cultures. Due to the mucoid, spreading nature of the colony, contaminants may be incorporated into the growth which are hard to eliminate. Usually repeated streaking on E.M.B. plates will eliminate the contaminant.

SEROLOGY

The details of the complement-fixation test for scleroma appear elsewhere.[8] The antigen used in this test is a strain of *K. rhinoscleromatis* isolated from a patient having scleroma. After cultivation for seven days in nutrient broth containing 5 per cent dextrose, the bacteria were removed by centrifuging. The supernatant liquid was discarded and the bacilli were washed in 0.85 per cent saline solution. A heavy suspension of the washed organism was made, exposed to a temperature of 65° C. for 30 minutes and suspended in a solution of Merthiolate (1:5000) in 0.85 per cent sodium chloride. The anticomplementary titre of the suspension was determined, and the final dilution of the antigen was made to give a negative antigen control. The actual titration was carried out according to the method of the quantitative Kolmer Wassermann.

Using the methods just described, 11 sera from patients with scleroma gave strongly positive reactions in relatively high dilution. A total of 534 sera from individuals not having scleroma were tested in the same way. Of these, 15 or 2.8 per cent gave positive reactions. All but two of these 15 showed a titre of less than 1:10. Additional work is needed to establish the test, but we feel that on the basis of the evidence submitted the complement-fixation test, if the result is positive, is of considerable value in establishing a diagnosis. The possible occurrence of negative results in early cases of scleroma must await further study.

CASE STUDIES

One further controversial question concerning scleroma has been its contagiousness. Its endemic nature has been suggested previously. Familial occurrence would indicate an infectious trait. Lasagna,[6] Robertson and Secretan,[12] and Gerber[4] have reported duplicate cases occurring in the same family. We have studied seven cases, six of which have occurred in the same family.

Case 1.—A 20-year-old male of Mexican descent was referred to the clinic because of dyspnea and a cough productive of a thick yellow mucoid material.

About one year before he had begun to notice that his nostrils were "plugged up" and that a sticky yellow discharge was chronically present. The significant physical findings related to the respiratory tract. A hard granulomatous mass filled the nares, nasopharynx, and the pharynx. In some places the mass was covered by dirty, green, malodorous crusted material which was occasionally expectorated. The voice was hoarse and there was some granulation involving the epiglottis and aryepiglottic folds. The patient complained that the dyspnea interfered with normal activity. There were no other significant laboratory or physical findings.

Biopsy of the lesion was taken from the middle turbinate. Thin stratified squamous epithelium without rete pegs or papillae covered a granuloma composed of loosely arranged fibroblasts and newly formed capillaries. A large proportion of the granuloma was made up of diffusely scattered Mikulicz cells giving the section a lacy appearance. The cellular infiltrate consisted of many plasms cells, a few lymphocytes and mononuclears and an occasional polymorphonuclear. Numerous Russell bodies and hyaline cells could be seen. Numerous bacilli could be demonstrated extra- and intracellularly by special stains. This picture was characteristic of the proliferative stage of scleroma.

From the above patient we isolated the scleroma bacillus in 20 consecutive throat cultures on blood agar and E.M.B. agar. The organism grows as a large, mucoid, flowing colony easily picked from the usual throat contaminants after 24 hours of incubation.

On questioning this first patient, we found that his father had similar symptoms, of longer duration. A report of the father follows:

Case 2.—The patient was 37 years of age. He had been essentially well until his nose was broken about ten years ago. After this his nose became progressively "stuffy" and a thick yellow discharge developed. Rhinoscleroma was diagnosed clinically elsewhere one year after onset and x-ray therapy was given. At the time of our examination, there was adequate airway, but the lining of the nose and pharynx was hard, irregular, and studded with foul-smelling, greenish crusts.

Biopsy taken from a warty growth on the pharyngeal wall showed a network of squamous epithelial cells enclosing cross sections of papillae. The epithelial cells were quite large with small dark staining nuclei and very prominent intercellular bridges. The papillae contained small capillaries, Mikulicz cells, a few lymphocytes, plasma cells and an occasional Russell body.

Two months after the above described biopsy was taken, considerable tissue was removed from the nose to reestablish airway which had become obstructed. Sections were made from tissue removed from the middle turbinate, posterior nares and lateral wall of the pharynx. These sections showed the cicatricial changes of the final stage of scleroma. There was atrophy of the epithelium which was stratified squamous. The submucosa was replaced by heavy collagenous fibers in a disorderly arrangement. There were a few atrophic mucous glands. One of these sections showed some granulomatous tissue with Mikulicz cells but almost all of the granuloma had been replaced by sclerotic tissue. Frisch bacilli were repeatedly isolated from cultures of the nose and throat.

After seeing that the father and son both were suffering from the same disease, we thought that other members of the family might show symptoms of a similar nature. From our discussion with father and son, we knew that they were suffering from vague symptoms associated with the upper respiratory tract. In addition to the son (Case 1) the family consisted of four daughters, a young son, aged nine, and the wife of the oldest son (Case 1). The mother of the children had been separated from the family for the past four years and was not available.

The wife of the patient in Case 1 and the youngest son were free of symptoms and culturally negative. The four girls seemed to show various stages of an infection of the nasopharynx which resembled the "diffuse" type of scleroma described by Szmurlo, and mentioned previously. Their case histories follow:

Case 3.—A girl, aged 19, was asymptomatic except for frequent "head colds" and a watery nasal discharge which had been chronically present for two years. There was marked atrophy of the inferior and middle turbinates and the nose contained crusts and casts of green-yellow matter that had the same foul odor noticed in others of her family.

Biopsy sections showed a granuloma infiltrated with a few lymphocytes, plasma cells, mononuclear cells and eosinophiles. There were numerous hyaline cells and a few isolated Mikulicz cells. Most of the surface was covered with stratified sciliated columnar epithelium. Numerous mucous glands were present. Characteristic organisms were isolated from cultures of the nose and throat.

Case 4.—The patient, a 17-year-old girl, was asymptomatic except for a chronic cough which she attributed to a thick, sticky, nasal and postnasal discharge. She had had "lobar pneumonia with empyema" three years ago and recovery had followed open drainage. Physical examination of the upper respiratory tract showed marked atrophy of the inferior and middle turbinates with some thickening of the septum superiorly and anteriorly, and the presence of greenish crusts.

Biopsy was taken from the anterior tip of the middle turbinate. The slightly irregular surface was covered on one side by stratified squamous epithelium, on the other by stratified ciliated columnar epithelium. There were many glands surrounded by loose connective tissue. The gland acini were small, the cytoplasm was pink and somewhat granular and the nuclei were small and dark. The lumina of the glands were small and appeared empty. There was moderate infiltration with plasma cells, lymphocytes and eosinophiles. There were a few vacuolated cells which possibly were Mikulicz cells. Characteristic organisms were isolated from cultures of the nose and throat.

Case 5.—The patient, a girl of 14 years, complained of increased nasal "stuffiness" of 18 months' duration, with no visible discharge. Physical examination showed almost complete obstruction due to the involvement of the anterior and of the inferior turbinates. The hypertrophied tissue causing obstruction had the appearance of granulation tissue and bled easily on touching. There was some crusting due to greenish yellow purulent exudate.

Biopsy was taken from the vestibule. The tissue consisted of a granuloma densely infiltrated with plasma cells. There were also some lymphocytes and neutrophiles. The surface was covered with a crust of necrotic exudate. There were a few islands of squamous epithelium beneath the crust. A few vacuolated cells, possibly Mikulicz cells, were present. The picture was that of a nonspecific granuloma. Repeated cultures showed the presence of scleroma bacillus. The lesion was that of early scleroma.

Case 6.—The patient was an 11-year-old girl who was asymptomatic although her sisters complained that she was always clearing her throat. Examination showed considerable hypertrophy of the tonsils. No atrophy, granulation or crusting was present in the nares.

(There is no record of a biopsy having been taken.)

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The findings in the last four cases, in our opinion, present pictures resembling varying stages of rhinoscleroma. In none of these cases were the symptoms sufficiently severe to result in the patient being referred to a doctor, yet physical examination revealed lesions which, at least in three of the cases, were suggestive of the disease. In one patient, the youngest sister, there were practically no gross pathologic lesions. The microscopic picture in all the other cases confirmed the existence of the disease syndrome, which, together with the isolation of the scleroma bacillus in each case, gave extremely presumptive evidence that here we had a family in which six members were afflicted with various stages of the disease rhinoscleroma. Serological findings in each of these cases gave further supporting evidence, although until the complement-fixation test, mentioned previously, is standardized, emphasis on the serology must be avoided.

SUMMARY

Scleroma is an infectious disease which is endemic in Southern California and must be considered in diagnosing lesions of the respiratory tract. The diagnostic procedure includes bacteriological, serological, and histological examinations. The bacteriological findings are positive in all stages of the disease. In early cases of scleroma the histologic appearances may not be pathognomonic. Identification of early scleroma by serologic tests has not been worked out. All of the advanced cases studied have been found to give positive reactions to complement-fixation tests. The proper evaluation of the information revealed by these three tests is diagnostic.

Discussion by H. James Hara, M.D., *Los Angeles*

Six of the seven patients mentioned in this paper I have seen. These six patients are one family—father, son and four daughters. They were all born in Colorado of Spanish, French, Indian, and Mexican ancestry and have lived in California since 1942. I know of no other instance in which there were so many cases in one family.

From 1893 to date 104 cases have been reported in the literature in the United States and one from Canada. Sixteen of the patients were born in the United States.

Clinically, two types are recognized. In the first group the characteristic lesion is a chronic granuloma invading the mucous membrane of the respiratory tract. The initial site of invasion is usually in the nose and progressively spreads to the nasopharynx, pharynx, larynx, trachea, and even to the bronchus. In some instances the larynx has been reported to have been the site of the primary lesion. In the second group the conspicuous lesion is in the skin area of the nasal vestibule, extending into the upper lip and protruding fairly firm masses without ulceration over the lower portion of the external nose. The lesions begin in the mucous membrane of the nose as a chronic granuloma and spread to the skin.

Three diagnostic criteria are:

1. Culture and isolation of Frisch organism.
2. Complement fixation.
3. Biopsy in later stage.

With the aid of laboratory workers scleroma can be accurately recognized long before the clinical diagnosis is possible.

Streptomycin is the specific: 0.5 gm. is given as an aerosol inhalation. Two gm. daily intramuscularly in four divided doses are given each day for 10 days. In one of our patients the organism disappeared on the seventh day.

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CASE REPORTS

◀ Eosinophilic Granuloma of Bone with Diffuse Pulmonary Involvement ◀ Dissecting Aneurysm

Eosinophilic Granuloma of Bone with Diffuse Pulmonary Involvement

Douglas D. Dickson, M.D., *Oakland*

IT is possible that Hand-Schuller-Christian's Disease, Letterer-Siwe's Disease and eosinophilic granuloma represent different phases of similar pathologic entities.

Various explanations have been given as to the etiology of this group of diseases. Rowland's studies[7] in 1928 led him to believe the causative factor was disturbed lipoid metabolism. Sosman[8] also classified xanthomatosis as a disease of lipoid metabolism. Jaffe and Lichtenstein[4] have concluded from their studies that eosinophilic granuloma of bone, Letterer-Siwe's Disease and Hand-Schuller-Christian's Disease may be considered different clinico-anatomic expressions of the same disease.

Green and Farber[2] point out the similarity between roentgenographic and histopathologic findings demonstrated in Hand-Schuller-Christian's Disease, Letterer-Siwe's Disease and eosinophilic granuloma.

In four of Rowland's cases of xanthomatosis, (Hand-Schuller-Christian type) that came to autopsy, a marked degree of pulmonary fibrosis was observed. Currens and Popp[1] report a case of xanthomatosis (Hand-Christian-Schuller type) with pulmonary fibrosis.

Imler[3] reports two cases of eosinophilic granuloma (reticulo-endotheliosis) with pulmonary manifestations, one of which represented the Hand-Christian-Schuller type.

Pulmonary lesions secondary to eosinophilic granuloma must be a rare manifestation of a fairly common disease. Numerous case reports of eosinophilic granuloma without the pneumonic lesions have been reported since Jaffe and Lichtenstein[5] and Otani and Ehrlich[6] almost simultaneously described the new entity.

Following is a case report of eosinophilic granuloma with pulmonary manifestations.

CASE REPORT

A 30-year-old white male was first examined in June, 1946. Four years previously there had been an injury to the left shoulder. In 1942 roentgenograms of the left shoulder revealed a cystic lesion of the acromion. (These roentgenograms were made elsewhere.) Symptoms subsided in a few days. Shortly thereafter, the patient applied for admission to the armed services and was rejected for "silicosis." For one year before our examination there had been pain along the inner side of the left thigh. One month before examination, dull aching pains in the region of the left hip had begun.

There was no history of exposure to silica. The patient was a healthy appearing white male and, except for tenderness overlying the left greater trochanter, physical examination disclosed no abnormalities.

Specific gravity of the urine was 1.016. There was no albumin or sugar and results of microscopic examination were negative. A Bence-Jones protein determination was normal.

Erythrocytes numbered 4,450,000 and leukocytes 10,550 for each cubic millimeter. There were 1 stab and 59 segmented neutrophils, 39 lymphocytes, and 1 eosinophil. The sedimentation rate was 18 mm. in 1 hr. 5 min. A sternal puncture* revealed increased eosinophils. Result of a Wassermann test was negative. Serum calcium was 11.4 mg. per cent and serum phosphorus 3.5 mg. per cent. Acid phosphatase was 2.0 King-Armstrong units and alkaline phosphatase 6.8 King-Armstrong units. Serum albumin measured 5.27 gm. per cent and serum globulin 1.63 gm. per cent. Electrocardiographic tracings were within normal limits. Roentgenograms (Figures 1 and 2) revealed cystic areas in the left acromion, in the first sacral segment, in the ischium about the acetabulum and in the region of the left greater trochanter.

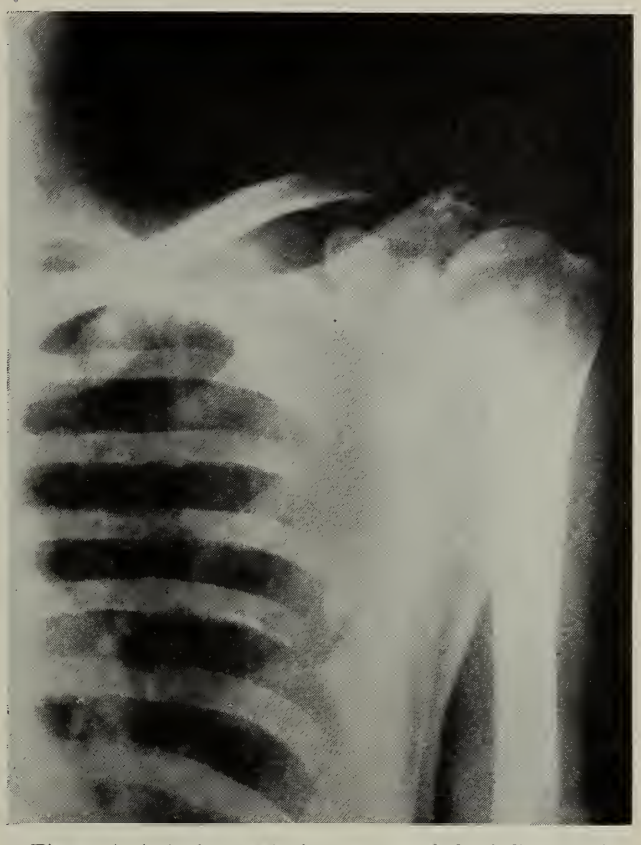


Figure 1. Anterior-posterior x-rays of the left acromion demonstrating cystic changes in the acromion process.

On the right, cystic areas were present in the ischium. There was also a destructive lesion in the adjacent margins of the 12th thoracic and first lumbar vertebra.

Chest films (Figure 3) revealed a diffuse infiltration of both lung fields. There were a few Gram positive rods in the sputum, numerous pus cells and rare eosinophils.

A biopsy was done on the lesion of the left femur. Yellowish gelatinous material was encountered. Microscopic sections (Figure 4) showed the tissues to be made up of connective tissue cells, some of which contained vacuoles in which lipoid material had been deposited. These connective tissue cells (histiocytes) gave a granulomatous appearance to the tissue. Eosinophilic leukocytes were present in enormous number, and there was an occasional giant cell. Numerous areas of necrosis were present in the section.

*We are indebted to Dr. Ernest Falconer for his opinion with reference to the examination by means of sternal puncture.

From August 6 to September 2 x-ray therapy was given to the lesion involving the left shoulder, the right lung, the left ilium and the left upper femur, administered in the following manner.

Right anterior chest: Field 15-17 cm. 200 k.v.p., (Filter ½ mm. cu. and 1 mm. al.). Skin target distance 70 cm. Four treatments totalling 1014 r.

Left shoulder posterior portion: Field 15-17 cm. 200 k.v.p. (½ mm. cu. 1 mm. al.). Skin target distance 70 cm. Six treatments totalling 1014 r.

Left ilium and left upper femur: Field 15-17 cm. 200 k.v.p. (Filter ½ mm. cu. 1 mm. al.). Skin target distance 70 cm. Six treatments totalling 1014 r.

Roentgenographic examination of the chest on October 29. 1946. revealed no improvement so far as the lungs were concerned. However, marked improvement could be demonstrated in the roentgenogram of the ilium and the left femur, with considerable evidence of sclerosis of the cystic areas.



Figure 2. Anterior-posterior x-rays of pelvis demonstrating cystic lesions in the ilium and left greater trochanter.

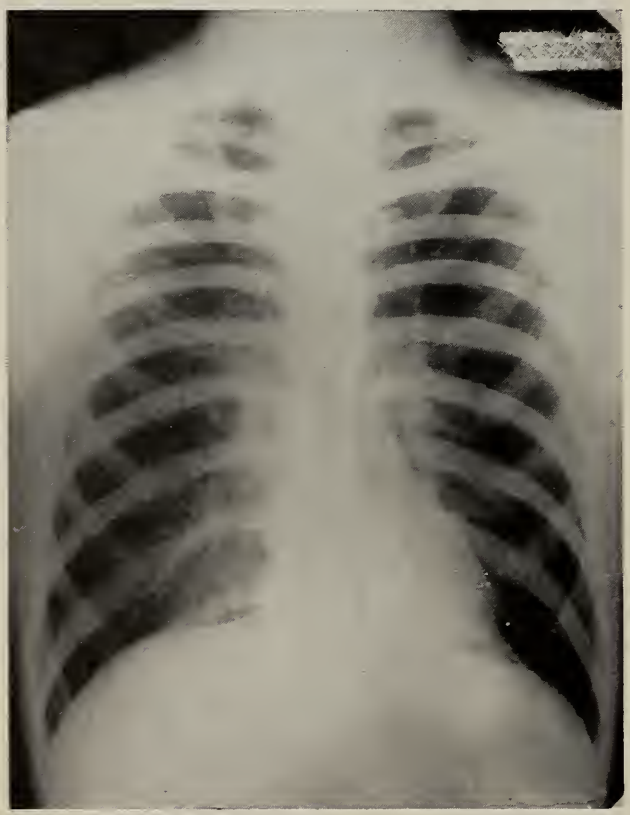


Figure 3. Anterior-posterior x-rays of the lungs revealing diffuse infiltration of both lung fields.

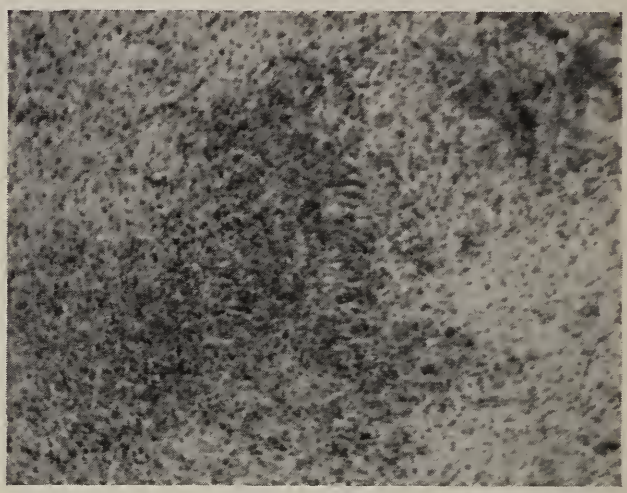


Figure 4. Microscopic examination of tissue removed from left greater trochanter revealing histiocytes and eosinophilic leukocytes.



Figure 5. Anterior-posterior x-rays of the left ilium and left greater trochanter demonstrating the regeneration of bone at the site of the cystic areas involving the ilium and left greater trochanter following x-ray therapy to the ilium, and excision and transplantation of iliac bone chips to the cyst in the left greater trochanter.

both in the ilium and the left greater trochanter (Figure 5).

This case has been reported because of the pneumonic manifestations associated with extensive osseous lesions characteristic of eosinophilic granuloma.

426 Seventeenth Street.

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Dissecting Aneurysm

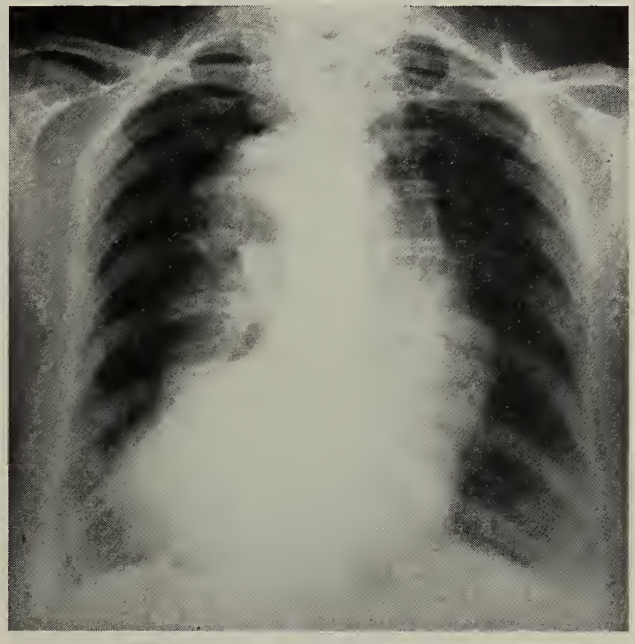
Morrill L. Ilsley, M.D., *Claremont*

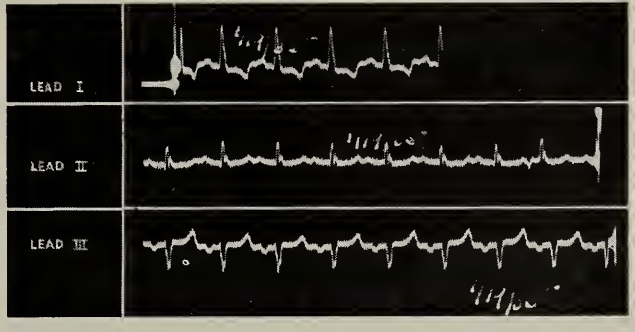
DISSECTING aneurysm of the aorta rivals syphilis in the number and variety of disease entities which it may simulate, and with which it may be confused. It occurs more frequently in men than in women, and usually in patients with preexisting hypertension. Erdheim's medial necrosis is the primary lesion in some cases, and dissection results by virtue of hematoma formations within the wall of the aorta. Primary rupture of the intima and subsequent dissection of the media also occur in the absence of preexisting medial necrosis.

The diagnosis is made by the location of the pain, which is often excruciating. It frequently resembles distress in the chest produced by coronary thrombosis, but does not radiate to the arm. It does tend to radiate to the back, between the scapulae, and sometimes to the neck and head, lower back and legs. It may be throbbing in character and intermittent. The physical findings are variable. The blood pressure does not drop, unless the patient develops the signs and symptoms of shock. The sudden development of a diastolic murmur of aortic insufficiency accompanied by the increased pulse pressure may appear. Roentgenography and fluoroscopy of the chest are most helpful, showing a widening of the aorta, especially in the oblique view. The electrocardiogram does not change materially. The Wassermann reaction, when positive, serves more often than not to confuse the diagnosis. The prognosis is somewhat better than in the case of coronary thrombosis if outcome is not immediately fatal. The treatment consists of rest in bed during the acute stage with repeated doses of morphine.

CASE REPORT

The patient, a woman aged 71 years, on October 15, 1934, ate half a watermelon and a whole chicken at one meal. She awoke the next morning in a clammy sweat with severe sharp pain in the upper left thoracic region posteriorly. Heart sounds were regular but distant. The blood pressure was 112 mm. systolic and 76 mm. diastolic; three days later it was 202 mm. systolic and 112 mm. diastolic. Urinalysis showed 2 plus albumin with hyaline and granular casts. The Wassermann reaction was positive. On October 23 erythrocytes numbered 4,080,000, with hemoglobin 57 per cent, and leukocytes numbered 8,950. The non-protein nitrogen on October 17 was 43.8 mg. per 100 cc., and on October 21 was 65.3 mg. per 100 cc. The blood sugar on October 17 was 160.0 mg. per 100 cc. and on October 21 was 85.4 mg. per 100 cc. Later determinations of the blood sugar were persistently high. On November 20, a roentgenogram showed a large aneurysm of the ascending aorta and of the arch of the aorta present with enlargement of the heart (Figure 1). An electrocardiogram showed inverted T1 (Figure 2). The non-protein nitrogen remained elevated. Much pus appeared in the urine on February 12 with accompanying rise of temperature, pain and tenderness in the right side of the abdomen. Vomiting was severe. A mass was felt by bimanual examination in the right lower quadrant of the abdomen.





A hemorrhagic ovarian cyst was the diagnosis. The leukocyte count was elevated to 16,900 with 89 per cent polymorphonuclear cells, of which 55 per cent were early forms. Vomiting persisted. Edema appeared. The patient became more and more stuporous and finally died March 8, 1935. Through the course of the illness, there was some precordial distress but none as severe as at the time of the onset.

Anatomical diagnosis*: healing dissecting aneurysm of aorta; medial necrosis idiopathica cystica of Erdheim; high grade atherosclerosis of aorta and major branches; benign nephrosclerosis; generalized arteriolarsclerosis (hypertension); marked hypertrophy and dilatation of heart; obliterative fibrous pericarditis; generalized passive congestion; anasarca moderate; high grade cerebral sclerosis; softening in left parietal cortex and in right lobe of cerebellum; chronic

*By Dr. Alvin Foord, Pasadena.

periappendiceal abscess well walled-off; purpuric hemorrhages in skin; atrophy of thyroid; obesity chiefly girdle type in distribution; diverticulum of sigmoid; steatosis of pancreas; small area of necrosis in pancreas (vascular in origin); chronic cystitis and pyelonephritis; cyst of right ovary; fatty infiltration of liver.

The heart was markedly enlarged and measured in the fixed specimen 12 cm. across and 13 cm. in length. The apex was formed exclusively by the left ventricle. There was considerable dilatation of all the chambers. The valves were free from change. Congenital defects were absent. The pulmonary and aortic orifices were markedly dilated. There was no evidence of fibrosis in any part of the organ, nor was any fresh necrosis seen. The left ventricle muscle was profoundly hypertrophied and measured from 15 mm. at the apex to 25 mm. at the base. The right ventricle muscle was only 3 to 4 mm. There was a large amount of fat in the epicardium, which extended somewhat into the muscle. The coronary vessels were very large, the left main coronary showing a lumen fully 6 mm. in diameter, and the major trunks were hypertrophied, consistent with the size of the heart. There were a few calcified plaques and a diffuse stiffening but no evidence of any encroachment upon the lumen, and no thrombosis was present.

Of particular interest was the aorta. The ascending portion and the arch showed much dilatation, and a baseball easily could have been put in the pocket just above the aortic valve. The intima, however, was glistening and smooth, and there were none of the ordinary signs of lues in this portion. The aortic leaflets were free from involvement and were soft and pliable. Just at the arch and to the right was a sacculated portion with an orifice about 4x4 cm., forming a mass about the size of half an egg, which was filled with organized blood clot. A smaller, similar dissecting pocket was noted on the posterior wall about the level of the origin of the innominate artery, forming a sac about 2x1 cm. The edges of both of these pockets were rolled and perfectly smooth and glistening and almost of the consistency of cartilage. Just above the left leaflet of the aortic valve was a third pocket showing dissection with pocket formation within the wall of the aorta, measuring about 2x2 cm. From this extended a crevice where the intima had obviously been separated and the defect filled in with a pink or white scar tissue, extending upward for a distance of about 8 cm., and from this similar evidence of old tears extended into the two pockets just described. The intima above these was smooth and glistening, and there was practically no plaque formation. There were numerous atheromatous and hyaline plaques at the arch and particularly at a point just below the arch, where an egg-shaped saccular aneurysm about 2 cm. deep was found. This measured about 5 cm. in diameter, the wall was thin, and the surface was covered by organized thrombus. Calcium plaque formation was found in this portion. Evidence of old laceration of the intima extended transversely and practically around the aorta at this level. Below this the aorta was diffusely dilated, tortuous, showing some longitudinal wrinkling, but primarily large yellow and hyaline plaques with small areas of calcification. Below the diaphragm there was profound tortuosity and not much dilatation. The major branches showed also profound tortuosity, marked plaque formation, and some calcification. The circumference at the extreme arch was about 9 cm. and at the diaphragm 7 cm.

COMMENT

Taylor and Morehead discussed the rupture of the aorta which occurs without the formation of a dissecting aneurysm. This occurs more frequently than is usually realized. Ash suggests that the study of the circulatory changes in the right arm with the observation of superior mediastinal obstruction and absence of pulse in the right carotid and right subclavian arteries leads to the correct diagnosis and localization of the lesion. Wainwright comments on the present-day tendency to diagnose as coronary thrombosis all conditions even remotely simulating it. Such a condition might well be a dissecting aneurysm. He reports an instance of coronary dissection resulting in occlusion of the vessel with a diagnosis of dissecting aneurysm before death. Ritvo and Votta commented on the value, in establishing the diagnosis, of roentgen studies showing increase in the width of the shadow of the aorta, cardiac hypertrophy, pericardial effusion and fluid in the pleural space. Leonard stated that the dictum was that "dissecting aneurysms caused by trauma are rare" but he presents a case of a patient who had one following an automobile accident. He said that the diagnosis of dissecting aneurysm must be differentiated between coronary thrombosis, perforated peptic ulcer, and acute pleurisy. Blain, Glynn and Hiratzka state that dissecting aneurysm of the abdominal aorta may, by involving one or both renal arteries, produce a urologic syndrome simulating acute nephrolithiasis or other urinary disorder. Sacks showed electrocardiogram changes seriatim, showing the possibility of great diagnostic value in the T-wave changes. Giles reported the case of a patient with a dissecting aneurysm of the femoral artery of undetermined cause, but with unusual symptoms, in which a cure was effected by ligation and a Matas aneurysmorrhaphy. Kinney, Sylvester, and Levine present a report of a case of coarctation of an aorta with a dissecting aneurysm in a 23-year-old pregnant white woman which was diagnosed before death. Henley and Gariepy report a case of dissecting aneurysm of the thoracic aorta diagnosed during life and proved at autopsy.

SUMMARY

Dissecting aneurysm of the aorta simulates and is often confused with many other disease entities.

There is no single diagnostic guidepost which is conclusive, and there may be broad variations in combinations of signs.

The case of a patient in whom the disease was diagnosed ante mortem is reported, together with a detailed anatomical diagnosis by the pathologist.

111 Indian Hill Boulevard.

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CLINICAL SYMPOSIUM

Prepared under the direction of Edgar Wayburn, M.D., *San Francisco*, and Clarence J. Berne, M.D., *Los Angeles*

Treatment of Bronchiectasis and Chronic Lung Abscess

Medical Aspects:

Clyde C. Greene, Jr., M.D.

Surgical Aspects:

Victor Richards, M.D.

THE term "chronic nontuberculous pulmonary suppuration" is used to denote a group of lung affections of mixed bacterial origin, with anerobic organisms frequently predominating, in which sufficient damage has occurred to the pulmonary parenchyma and bronchial tree to prevent complete and spontaneous resolution. Chronic pulmonary suppuration, regardless of the type, may be manifested clinically by cough, abundant sputum, fever of varying degree, anorexia, malnutrition, weakness, hemoptysis, and recurrent bouts of pneumonitis, but it must be remembered that these diseases are protean in their manifestations and extensive disease can exist without noteworthy clinical evidence of disease.

In this symposium the newer concepts of the pathogenesis and therapy of two types of chronic suppurative pulmonary disease, namely bronchiectasis and lung abscess, will be discussed. These conditions, however, may co-exist to varying degrees in the same area of diseased lung.

Bronchiectasis

Both medical and surgical measures are essential in the adequate therapy of bronchiectasis. Perry and King,[9] Alexander,[1] and others agree that about 50 per cent of all patients with bronchiectasis do not have surgical operations. A few in this group should have operations but refuse, while others have so little or so much disease as to contraindicate surgical treatment. The remainder suffer from severe unrelated disease prohibiting operations which otherwise are indicated.

Because of this large group of patients, tremendous interest has been centered on the "nonsurgical" management of the disease. The keynotes of this regimen are drainage, control of infection and the improvement of general health, both mental and physical.

Expulsion of the sputum is best obtained for these patients by postural drainage, which must be a regular part of the life of the medically treated patient and is best carried out from a high bed or table with complete vertical dependence of the trunk. Extreme flexion of the body, as described by Alexander,[1] is also of value when the patient is still able to carry out his normal occupation. Cough depressants reduce the efficacy of postural drainage and should be avoided, while simple expectorants such as ammonium chloride may be of assistance in promoting drainage.

Control of infection will not produce cure but when properly done will shorten the duration of acute exacerbations and make life more pleasant for the patient. Penicillin, both by inhalation and intramuscular techniques, has assumed a dominant role in the control of infection, but is of principal value when used for short periods to control the acute flare-ups that so regularly appear. In our experience the sulfonamides have been of little value, but success with long continued usage of sulfadiazine in a dosage of 1 gm. daily has been reported.

Other factors in the control of infection and the maintenance of good general health are adequate nutrition, avoidance of severe exposure, change to higher and drier climate (in some cases), and physical and mental adjustment to the disease.

By use of these measures the surgical treatment of bronchiectasis is made more effective and the patient who is not operated upon has an improved prognosis. In fact, Perry and King[9] estimate that 38 per cent of their non-surgical patients now have an excellent working-living capacity.

Thoracic surgeons and internists agree, however, that the best definitive treatment for bronchiectasis is surgical resection of the involved pulmonary tissue. As stated before, this is not feasible in all cases, but today it is possible, with a mortality of less than 5 per cent, to remove all but two of the five usual pulmonary lobes for the complete extirpation of bronchiectatic lung tissue.

The study of Perry and King[9] showed a 12-year mortality of 26 per cent in a group of 4,000 nonsurgical patients, with 41 per cent of these deaths occurring within five years after the onset of the disease. Hinshaw and Schmidt[5] have estimated that less than 10 per cent of patients with true bronchiectasis are benefited appreciably by medical treatment alone, and they judge the mortality rate in 15 years after diagnosis to be from 30 to 50 per cent. The younger the patient at onset, the poorer the prognosis without surgical treatment, so that it is particularly important to accurately evaluate bronchiectasis in children and to operate early in all suitable cases. Major thoracic operations are withstood well by children.

Complete visualization of the tracheo-bronchial tree by lipiodol bronchography is essential before resec-

From the Departments of Surgery and Medicine, Stanford University School of Medicine.

tion in cases of bronchiectasis. This reveals the degree and extent of pulmonary involvement, and decision as to the amount of pulmonary tissue to be resected must rest solely upon this diagnostic technique. Often the lung tissue appears grossly normal and the extent of the disease cannot be determined by the examining finger so that a preoperative decision as to the amount of tissue to be extirpated must be made.

In this regard several important contributions have been made by Churchill and Belsey,[3] Blades and Kent,[2] and Overholt and Langer.[8] Churchill and Belsey predicated that the essential architectural unit of the lung was not the lobe but the cluster of bronchopulmonary segments comprising a lobe. Each bronchopulmonary segment has now become more or less a surgical unit, and recent efforts at maximum conservation of good pulmonary tissue and function have been directed at segment resections of bronchopulmonary units whenever practical. Successful segmental resection involves detailed knowledge of the anatomy of the pulmonary lobe, but, briefly, it is accomplished by isolating and occluding the involved bronchus, noting the demarkation of the lobule from the remainder of the lobe, dividing the segmental pulmonary vessels, and then stripping the segment from the lobe by dividing the visceral pleura and following normal cleavage planes. Bleeding points on the lung surface are controlled by packs and ligatures.

* * *

Chronic Abscess of the Lung

Pulmonary abscess, acute and chronic, results from many causes, including aspiration, septic emboli, bronchial obstruction of any type, infection within a pre-existing cyst, or from foreign bodies which enter through the chest wall. Of these, aspiration is by far the most important.

The cause will of course affect the pathologic characteristics of lung abscess, but the majority result from the obstruction of a peripheral bronchus by infected material with destruction and disintegration of the involved bronchopulmonary segment. The abscess, which is usually single, is surrounded by an area of compressed and avascular lung tissue. Usually this causes adjacent pleural adhesions which seal off the pleural space immediately over the abscess, and results in bronchial communication, due to dissolution or dislodgment of the obstruction or to sequestration of necrotic lung tissue.

Signs of chronic abscess of the lung develop within three weeks after the onset of an acute abscess, which is of short duration. The acute phase is the optimal time for both diagnosis and treatment, and it is during this stage that non-surgical methods of treatment have their opportunity for cure. When chronic, a lung abscess is primarily a surgical problem, although here again best results have been obtained by combining adequate medical and surgical treatment.

The fundamental principle in any treatment of lung abscess, regardless of chronicity and the variability of the clinical manifestations, is adequate drainage. The medical therapy includes drainage, by either postural or bronchoscopic techniques, and drugs. Postural drainage here is of less value than bronchoscopic drainage since the latter permits more complete drainage, the removal of inspissated secretions, the administration of drugs, and, in some instances, the diagnosis of an unsuspected foreign body or neoplasm. Drug therapy today is primarily with penicillin, although in some instances the sulfonamides or streptomycin may prove of value.

If precise localization has been established, conservative treatment of chronic lung abscess is relatively safe because of the peripheral location and the local adherence of the visceral and parietal pleura. Neuhof,[7] in fact, states that the mortality rate of patients with lung abscess treated by early extensive drainage is less than 5 per cent. Samson's[10] concept is that therapy not resulting in both clinical and roentgenological evidence of improvement within two to three weeks should be abandoned. For these reasons external drainage by properly placed rib resection and cavernostomy should be instituted early to prevent irreparable change in the lung.

The advantages of pulmonary resection have been explored, primarily by Sweet,[11] Glover and Clagett,[4] and Lindskog.[6] The present trend is toward the replacement of external drainage by pulmonary resection in chronic abscess, or in any abscess complicated by irreparable lung disease. Glover and Clagett[4] in summation of the general surgical opinion, and as a result of their own experience with 37 cases, list these indications for such pulmonary resection:

1. Persistent symptoms secondary to pathological changes resulting from open drainage.
2. Multiple or multilocular abscesses.
3. Abscesses associated with secondary changes such as fibrosis, bronchiectasis, bronchiostenosis, or atelectasis.
4. Abscesses anatomically located in a position that prohibits drainage.
5. Abscesses in which the diagnosis of malignancy is considered.
6. Abscesses associated from their onset with excessive bleeding.
7. Abscesses in children.
8. Abscesses secondary to foreign bodies not removable by bronchoscopy.

Glover and Clagett report that in 21 cases in which conservative resection was done, there was one death—a mortality rate of 4.8 per cent. In 16 cases in which the lesion was so extensive that pneumonectomy had to be performed, there were six deaths—a mortality rate of 37.5 per cent; but in only seven of these cases, or 44 per cent, were good results obtained.

Future treatment of chronic lung abscess should be directed toward prevention, by means of prompt and adequate medical treatment or by early adequate external drainage, and resection, rather than dependence on repeated external drainages, plastic procedures, or thoracoplasty. The necessity for resection should be recognized and accepted and in many of

the "early" chronic cases, particularly if there is associated pulmonary disease, resection should take precedence over external drainage as the initial procedure.

* * *

To conclude, it may be said that the following developments made during the past 15 years have entirely altered the management and prognosis of the patient with chronic nontuberculous pulmonary disease:

1. Improvements in the diagnostic techniques, namely roentgenology and bronchoscopy.
2. Improvements in the control of infection by chemotherapeutic agents, namely penicillin, streptomycin and the sulfonamides.
3. Improvements in the control of shock from blood loss, permitting longer and more extensive surgical operation.
4. Improvements in the technique of intratracheal positive pressure anesthesia by which cardiorespiratory embarrassment incident to an open pneumothorax can be prevented.
5. Improvements in the technique of closure of a divided bronchus, preventing bronchial fistulae.
6. Improvements in the individual ligation technique in the management of major pulmonary vessels, preventing secondary hemorrhages.

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MEDICAL PROGRESS:

Isotopes in Clinical and Experimental Medicine*

Ellsworth C. Dougherty, Ph.D., M.D., and John H. Lawrence, M.D., Sc.D., *Berkeley*

This is Part I of an article in two parts. Part II, Important Applications of Isotopes in Experimental Medicine, will appear in the August issue.

INTRODUCTION

In 1898—now 50 years ago—the Curies discovered radium ($_{88}$Ra). Their announcement, following only two years after Becquerel's discovery of the natural radioactivity associated with uranium ($_{92}$U) salts, not only presaged a vast new era in physics, but also in medicine. Within a few years after the existence of radium was announced, it had come into use in clinical practice—in the treatment of certain malignancies and dermatoses. These uses of radium are examples of the application of isotopes to medical problems. The 50 years since the Curies' demonstration of the existence of radium have witnessed many advances in medicine as a result of such application.

The concept of the "isotope" did not develop, however, until work on the natural radioactive series—of uranium and thorium ($_{90}$Th) parentage—had been under way for several years. It was early recognized that the spontaneous decay of the heaviest elements behaved according to a regular pattern. During the first decade of the 20th century "elements" were discovered that had quite different decay characteristics, but were chemically identical. Thus radium and mesothorium 1 ($MsTh_1$) were found to be chemically inseparable, but to have quite different decay patterns—the former (as is now known) giving off alpha and gamma rays with a half-life of about 1590 years; the later, beta rays with a half-life of 6.7 years. The English physicist, Soddy, fitted these facts together and recognized that, at least among the heaviest elements, there could be two or more forms of a given element differing by nuclear mass. For these different forms of a single element he coined the name *isotope*.

The earliest isotopes were distinguished by their different radioactive properties, and all belonged to the three natural radioactive series of heaviest elements. But Soddy suspected that stable elements also might consist of mixtures of more than one nuclear form. He and his associates studied lead ($_{82}$Pb) from different sources; this element was known to be the end product of the natural radioactive series. They demonstrated quite clearly that lead in thorium ore was lighter than lead from other sources. By 1920 the existence of more than one nuclear form of a light element unrelated to the natural radioactive series was conclusively shown by the work of Aston with neon ($_{10}$Ne).

Today we know that all of the 96 elements so far discovered may exist in more than one nuclear form. Of the 81 stable elements 60 exist as more than one stable isotope. There are in addition over 600 known unstable species—at least one such isotope being known for each of the 96 elements. Only a small proportion of these exist in nature in detectable form. The others are *artificial* radioisotopes made in the laboratory principally by the cyclotron and nuclear pile reactor; all of these have been found since the discovery of artificial radioactivity by the Joliot-Curies in 1933.

The use of isotopes in medicine depends upon the exploitation of certain of their nuclear properties. For example, the radiations accompanying the decay of a few unstable isotopes have made possible their use in therapy. At the present time, radium is the best known example of an isotope of importance in radiotherapy. Strictly speaking, however, what we commonly call "radium" is only one isotope of the element $_{88}$Ra—the one characterized by a nucleus of 226 mass units and a long half-life (1590 years). In addition to $_{88}Ra^{226}$ there are also known the species $_{88}Ra^{223}$ (AcX), $_{88}Ra^{224}$ (ThX), and $_{88}Ra^{228}$ ($MsTh_1$) with half-lives of 11.2 days, 3.64 days, and 6.7 years respectively.

Much more important than the direct use of radioisotopes in therapy, however, is the application of isotopes as *tracers* in the study of living processes. It is possible to employ both stable and radioactive species in this manner. Artificial radioisotopes can be introduced into biological systems and their fate studied by following the distribution of the decaying atoms. Stable isotopes separated from their more abundant homologues or enriched in relation to these can also be introduced into biological systems and followed by studying the fluctuations in isotope ratios. With such tracers it has been possible to study many metabolic processes formerly unapproachable, even indirectly. The store of new knowledge made available with isotopes is already great, but the potentialities of these applications have been little more than touched.

The isotopes that have been used in fundamental investigations in medicine and related fields are listed with their principal applications in the accompanying Table 1. It is to be noted that only seven

From the Divisions of Medical Physics (Donner Laboratory) and Medicine, University of California, Berkeley.

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stable isotopes have so far found biological use. However, this list of stable species will unquestionably be somewhat expanded in the near future since the United States Atomic Energy Commission[144] has recently announced the availability in limited quantities of a number of additional separated isotopes. Most of the rare species of value in tracer work are heavier than the most abundant species of the same elements; hence the stable tracers are commonly referred to as "heavy isotopes." Altogether there are 278 known stable isotopes belonging to 81 elements; 197 of these are less abundant species of the 60 elements existing in more than one stable form. A good number of these will quite probably find biological application. From the accompanying table it may also be seen that over 70 radioisotopes have found biological application. Of the more than 600 known radioactive isotopes, about 160 have properties that adapt them to biological tracer work. Thus not quite half of the potentially valuable unstable species have so far been applied biologically. However, many of those remaining will doubtless be employed in the near future in tracer experiments. The availability of a large number of radioisotopes has been announced by the United States Atomic Energy Commission.[143]

Some of the important studies with isotopes are dealt with in the remaining part of this paper. It is not intended that our coverage be comprehensive. Aside from the role of radioisotopes in therapy the discussion will center around their use as tools for the elucidation of physiological processes. A truly comprehensive survey of tracer applications would cut across all the experimental fields of biology and inevitably separate in a somewhat artificial manner isotopic from non-isotopic studies of the same phenoma. However, tracer research is one of the most important aspects of modern experimental science, particularly biology (and therefore medicine); a survey of some of the more important achievements with isotopes is thus, we believe, of interest. It is hoped that the reader will thereby gain orientation in this rapidly growing and vital field. For reasons of limitation in space we are not dealing here with the theory and techniques of isotope production, use, and measurement. For detailed treatment of this subject in relation to radioisotopes we refer the reader to the recent book by Kamen[70] and that edited by Lawrence and Hamilton.[80] As yet, however, no detailed treatment of stable isotopes in biology exists in book form.

Of the two sections that comprise the remainder of this paper, the first deals with the clinical application of isotopes and the second with their application to problems in experimental medicine.

CLINICAL APPLICATIONS OF ISOTOPES

General Considerations:

Radium and radon ($_{86}$Rn), and their decay products, have been used for over 45 years in the treatment of various malignancies and dermatoses. These applications are familiar to the medical profession as a whole and need not be detailed here.

As indicated in Table 1 artificial isotopes of two elements, phosphorus ($_{15}$P) and iodine ($_{53}$I), have thus far been employed in therapy with definite success. Others—sodium ($_{11}$Na), manganese ($_{25}$Mn), zinc ($_{30}$Zn), strontium ($_{38}$Sr), yttrium ($_{39}$Y), zirconium ($_{40}$Zr), columbium ($_{41}$Cb), and gold ($_{79}$Au)—have received preliminary trial, but therapeutic techniques with these elements are still in the experimental stage. A number of isotopes have also been employed for diagnostic purposes. These are discussed in the following subsections.

The isotopes that so far have shown definite value in therapy and diagnosis have been those that demonstrate a fair degree of selective localization, as the result either of their normal fate in metabolism or of their fate as special compounds or colloids. Thus $_{15}$P concentrates to some degree in rapidly growing tissue (particularly in the nucleoprotein fraction) and in bone; $_{53}$I localizes in the thyroid gland (at least several hundred times the concentration in the rest of the body); and certain colloidal preparations can be made that localize in various parts of the reticuloendothelium or at the point of injection.

So far, all therapeutic techniques of radiation with isotopes, except for the treatment of hyperthyroidism with radioiodine, have suffered from the limited selectivity of uptake by the diseased tissue over normal tissues. For example, in the treatment of diseases of the bone marrow and lymphatic system with radioactive $_{15}$P it is impossible to avoid to a greater or lesser extent the irradiation in various parts of the body of those normal cells that metabolize rapidly and others in their immediate vicinity. Actually, in the treatment of polycythemia vera, for example, it would be desirable if irradiation could be delivered only to the nucleated red cells; and in lymphosarcoma and leukemia only to the offending leukocytes or lymphosarcoma cells, and not to the normal cells, especially the platelet and red cell producing centers. Some additional progress may be anticipated in the management of these blood dyscrasias by the application of labeled colloids. The work of Jones, Wrobel, and Lyons[68], and the more recent work of Dobson *et al.*[23], shows that radiation may be limited largely to the liver and spleen by the use of anhydrous colloidal chromic phosphate labeled with $_{15}P^{32}$, which localizes selectively in the reticuloendothelial cells of the liver and spleen when introduced intravascularly in a highly dispersed form. Similar properties have been found by Dobson *et al.*[22] for a number of other colloids—of $_{39}$Y, $_{40}$Zr, and $_{41}$Cb—which may be labeled with radioisotopes of these respective elements. Some of the colloids can be concentrated to a high degree in the bone marrow, others in the liver and spleen. Other colloids suggested are those of $_{25}$Mn (Hahn and Sheppard[48]; and Sheppard and Hahn[126]).

However, for neoplastic diseases in general, localizing substances of adequate selectivity that can be labeled and used for radiotherapy have not been

TABLE 1.—*Important Stable and Radioactive Isotopes That Have Been Used in Basic Medical and Related Investigations*‡

*Element	§Isotope		Some problems in which isotope has been used
	Stable	Radioactive	
*Hydrogen ($_1$H)	$_1H^1$		High speed proton irradiation (suggested) 150
	*$_1H^2$(D)		Intermediary metabolism, 70, 122; body water turnover, 61-63; and content, 63, 99
		$_1H^3$(T)	Body water content, 107; photosynthesis, 70
Lithium ($_3$Li)	$_3Li^6$ (in natural element)		Slow neutron therapy of experimental tumors, 73, 153
Beryllium ($_4$Be)		$_4Be^7$	Absorption, distribution, and excretion, 51
	$_4Be^9$ (in natural element)		Fast neutron irradiation and therapy, 1, 132
Boron ($_5$B)	$_5B^{10}$ (in natural element)		Slow neutron therapy of experimental tumors, 153
*Carbon ($_6$C)		$_6C^{11}$	Intermediary metabolism, 12, 119, 150, 151; CO distribution and elimination, 141; photosynthesis, 120
	*$_6C^{13}$		Intermediary metabolism, 12, 145, 150, 151
		$_6C^{14}$	Photosynthesis, 6; other preliminary tracer work, 8
*Nitrogen ($_7$N)		$_7N^{13}$	Respiratory gas exchange, 66; supposed nitrogen fixation by barley, 118
	*$_7N^{15}$		Intermediary metabolism, 145
*Oxygen ($_8$O)	*$_8O^{18}$		Photosynthesis, 121; bacterial fractionation, 24
Fluorine ($_9$F)		$_9F^{18}$	Bone and tooth physiology and chemistry, 147
*Sodium ($_{11}$Na)		$_{11}Na^{22}$	Retention in congestive heart disease, 112; effect of dietary chloride deficiency, 19
		$_{11}Na^{24}$	Electrolyte metabolism, 33, 34, 43, 45, 49, 54, 69, 92, 146; adrenal physiology, 3-5; therapy of leukemia, 85, 139
*Magnesium ($_{12}$Mg)		$_{12}Mg^{27}$	Photosynthesis, 117
*Phosphorus ($_{15}$P)		$_{15}P^{32}$	Mineral metabolism, 15, 16, 60; intermediary metabolism, 13, 41a, 59; therapy of chronic leukemias, polycythemia vera, etc., 29, 30, 65, 74-79, 82, 115, 148, and skin lesions, 88, 90; labeling of erythrocytes, 103; diagnosis of malignancy, 89, 91; colloids localizing in the reticuloendothelial system, 2, 22, 23, 67
*Sulfur ($_{16}$S)	*$_{16}S^{34}$		Intermediary metabolism, 26
		$_{16}S^{35}$	Intermediary metabolism, 95, 96, 134-137; thiamine metabolism, 10; mineral metabolism, 27, 129

Element	Radioactive Isotope	Some problems in which isotope has been used
*Chlorine ($_{17}$Cl)	$_{17}Cl^{38}$	Mineral metabolism, 45, 93
Argon ($_{18}$A)	$_{18}A^{41}$	Respiratory gas exchange; blood circulatory pattern, 66
*Potassium ($_{19}$K)	$_{19}K^{42}$	Mineral metabolism, 32, 43, 45, 105; adrenal physiology, 3-5
*Calcium ($_{20}$Ca)	($_{20}Ca^{41}$) $_{20}Ca^{45}$	Mineral metabolism, 42
*Manganese ($_{25}$Mn)	$_{25}Mn^{52}$ ($_{25}Mn^{54}$)	Distribution of colloidal MnO_2 in reticuloendothelial system, 48, 126
	($_{25}Mn^{52}$) $_{25}Mn^{54}$	Mineral metabolism, 44
	$_{25}Mn^{56}$	Mineral metabolism, 9
*Iron ($_{26}$Fe)	$_{26}Fe^{55}$ $_{26}Fe^{59}$	Mineral metabolism, 46, 47, 98; blood physiology, 37-39; and preservation, 35, 36, 116

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Element	Radioactive Isotope	Some problems in which isotope has been used
?*Cobalt ($_{27}$Co)	$_{27}Co^{56}$ ($_{27}Co^{57}$) $_{27}Co^{58}$	Mineral metabolism, 44
*Copper ($_{29}$Cu)	$_{29}Cu^{64}$	Mineral metabolism, 152
?*Zinc ($_{30}$Zn)	$_{30}Zn^{63}$	Interstitial injection of pectin-protected colloid, 102
	$_{30}Zn^{65}$	Mineral metabolism, 125
Arsenic ($_{33}$As)	$_{33}As^{74}$	Absorption, distribution, and excretion, 25, 64; experimental filariasis, 83
Selenium ($_{34}$Se)	$_{34}Se^{83}$	Absorption, distribution, and excretion, 94
?*Bromine ($_{35}$Br)	$_{35}Br^{82}$	Electrolyte exchange, 43, 45; thyroid physiology, 109; distribution of brominated dyes, 100
Krypton ($_{36}$Kr)	$_{36}Kr^{79, 81}$	Respiratory gas exchange; blood circulatory pattern, 66, 140
Rubidium ($_{37}$Rb)	$_{37}Rb^{86}$	Electrolyte exchange, 43
Strontium ($_{38}$Sr)	$_{38}Sr^{85}$	Absorption, distribution, and excretion, 51
	$_{38}Sr^{89}$	Bone physiology, 42, 50, 108
	$_{38}Sr^{90}$	Absorption, distribution, and excretion, 50
Yttrium ($_{39}$Y)	$_{39}Y^{88}$	Absorption, distribution, and excretion, 50
	$_{39}Y^{91}$	Absorption, distribution, and excretion, 50; colloids in reticuloendothelial system, 22, 23
Zirconium ($_{40}$Zr)	$_{40}Zr^{89}$	Absorption, distribution, and excretion, 51
	$_{40}Zr^{95}$	Absorption, distribution, and excretion, 50; colloids localizing in reticuloendothelial system, 22, 23
Columbium ($_{41}$Cb)	$_{41}Cb^{95}$	Absorption, distribution, and excretion, 50; colloids localizing in reticuloendothelial system, 22
Molybdenum ($_{42}$Mo)	$_{42}Mo^{99}$	Absorption, distribution, and excretion, 104
Ruthenium ($_{44}$Ru)	$_{44}Ru^{103}$ $_{44}Ru^{106}$	Absorption, distribution, and excretion, 50
Antimony ($_{51}$Sb)	$_{51}Sb^{124}$	Absorption, distribution, and excretion; experimental filariasis, 11
Tellurium ($_{52}$Te)	$_{52}Te^{121}$	Absorption, distribution, and excretion, 20
	$_{52}Te^{127}$ $_{52}Te^{129}$	Absorption, distribution, and excretion, 50
*Iodine ($_{53}$I)	$_{53}I^{128}$	Iodine metabolism and thyroid physiology, 84
	$_{53}I^{130}$ $_{53}I^{131}$	Iodine metabolism and thyroid physiology, 57, 84, 138; therapy of thyrotoxicosis, 14, 52, 56, 58; and metastatic thyroid carcinoma, 123, 124; absorption of insulin, 114
Xenon ($_{54}$Xe)	$_{54}Xe^{127}$	Respiratory gas exchange; blood circulatory pattern, 66; narcotic effects, 81
	$_{54}Xe^{133}$	Absorption and distribution, 50
Cesium ($_{55}$Cs)	$_{55}Cs^{134}$	Absorption, distribution, and excretion, 51
	$_{55}Cs^{135}$	Absorption, distribution, and excretion, 50
Barium ($_{56}$Ba)	$_{56}Ba^{133}$	Absorption, distribution, and excretion, 51
	$_{56}Ba^{140}$	Absorption, distribution, and excretion, 50
Lanthanum ($_{57}$La)	$_{57}La^{140}$	Absorption, distribution, and excretion, 50
Cerium ($_{58}$Ce)	$_{58}Ce^{141}$	Absorption, distribution, and excretion, 50
	$_{58}Ce^{144}$	Absorption, distribution, and excretion, 50
Praseodymium ($_{59}$Pr)	$_{59}Pr^{143}$	Absorption, distribution, and excretion, 50

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Element	Radioactive Isotope	Some problems in which isotope has been used
Element 61	$_{61}^{147}$	Absorption, distribution, and excretion, 50
Gold ($_{79}$Au)	$_{79}Au^{198}$	Absorption, distribution, and excretion, 28; chrysotherapy in arthritis, 7; colloidal therapy, 46a, 125a
Mercury ($_{80}$Hg)	$_{80}Hg^{197}$	Mercury vapor as an industrial health hazard, 40
Lead ($_{82}$Pb)	$_{82}Pb^{210}$ (RaD)	Absorption, distribution, and excretion, 17, 101
	$_{82}Pb^{212}$ (ThB)	Absorption, distribution, and excretion, 21
Bismuth ($_{83}$Bi)	$_{83}Bi^{210}$ (RaE)	Absorption, distribution, and excretion, 72
Astatine ($_{85}$At)	$_{85}At^{211}$	Thyroid physiology, 53
Radon ($_{86}$Rn)	$_{86}Rn^{220}$ (Tn)	Elimination in breath, 130
	$_{86}Rn^{222}$	Numerous studies on uptake and elimination in breath, distribution, etc.; treatment of various malignancies and dermatoses
Radium ($_{88}$Ra)	$_{88}Ra^{226}$ $_{88}Ra^{228}$ ($MsTh_1$)	Numerous studies on distribution, toxicity, etc.; treatment of various malignancies and dermatoses
Thorium ($_{90}$Th)	$_{90}Th^{228}$ (RdTh)	Absorption, distribution, and excretion, 50
	$_{90}Th^{232}$ (natural element)	Numerous studies on distribution, toxicity, etc.
	$_{90}Th^{234}$ (UX_1)	Absorption, distribution, and excretion, 50
Protoactinium ($_{91}$Pa)	$_{91}Pa^{233}$	Absorption, distribution, and excretion, 50
Uranium ($_{92}$U)	Natural element	Numerous studies on distribution, toxicity, etc.
	$_{92}U^{235}$ (AcU)	Production of slow neutrons, 128; effect of fission from colloids localizing in reticuloendothelial system, 142
Neptunium ($_{93}$Np)	$_{93}Np^{239}$	Absorption, distribution, and excretion, 50
Plutonium ($_{94}$Pu)	$_{94}Pu^{239}$	Absorption, distribution, and excretion, 50
Americium ($_{95}$Am)	$_{95}Am^{241}$	Absorption, distribution, and excretion, 50
Curium ($_{96}$Cm)	$_{96}Cm^{242}$	Absorption, distribution, and excretion, 50

‡See also the book by Govaerts (1945)[41] on the use of stable isotopes and the recent book by Kamen (1947)[70] and Lawrence and Hamilton (1948)[80] on the use of radioisotopes in biology.

*Elements known or believed to be essential in mammalian nutrition based on the book by Shohl (1939)[127]; those for which unanimity is lacking are also marked with a question mark (?).

§An isotope is placed in parentheses if it occurs together with another isotope (of the same element) used for tracer work, but is itself not significant for the tracer purposes to which the mixture may be applied. Two or more isotopes are connected by a brace if they occur together in tracer preparations and are of about equal importance.

found. If such are found, it would be desirable that they carry a radioactive isotope which emits a very soft ray, such as radiohydrogen ($_1H^3$) or long-lived radiocarbon ($_6C^{14}$). Even these emit beta-rays that traverse several cell diameters; however, the half-penetration of the $_1H^3$ beta-ray is less than the radius of the average cell.

Radiophosphorus ($_{15}P^{32}$) in Therapy and Diagnosis:

The first radioisotope to be used in therapy was $_{15}P^{32}$. It was employed as early as 1936 by Lawrence and associates[74] in the treatment of chronic leukemia and polycythemia vera. In the treatment of chronic leukemia, results with this isotope are good, and in the treatment of polycythemia vera, excellent, as brought out in the studies of a large group of patients treated since 1936[75-79, 82]. Other workers have later taken up similar studies, and there are reports by Reinhard *et al.*[115], Erf[29, 30], Warren[148], Jacobson *et al.*[65], and others. $_{15}P^{32}$ in soluble form (in labeled isotonic Na_2HPO_4) given by mouth or vein is used in the treatment of these blood dyscrasias. The determination and calculation of dosage, routes of administration, and supportive treatment of patients receiving this type of therapy are discussed in most of the works cited.

It is at the present time the treatment of choice for many cases of polycythemia (rubra) vera (i.e., primary polycythemia, erythremia, or Osler-Vaquez's disease). In most patients complete hematological remission and almost complete symptomatic relief can be effected. A single course of treatment may bring about a remission lasting many years. A recent analysis of end results in a series of 100 patients with polycythemia vera, and treated with $_{15}P^{32}$, [76-78], is very encouraging. The average age at onset of the disease in the group was 48. Administration of $_{15}P^{32}$ was necessary on the average of one course every three years, in order to keep the red cells at normal or near normal levels and for the relief of symptoms. In the group of 15 patients who have died from various causes, the average age at death was 67—

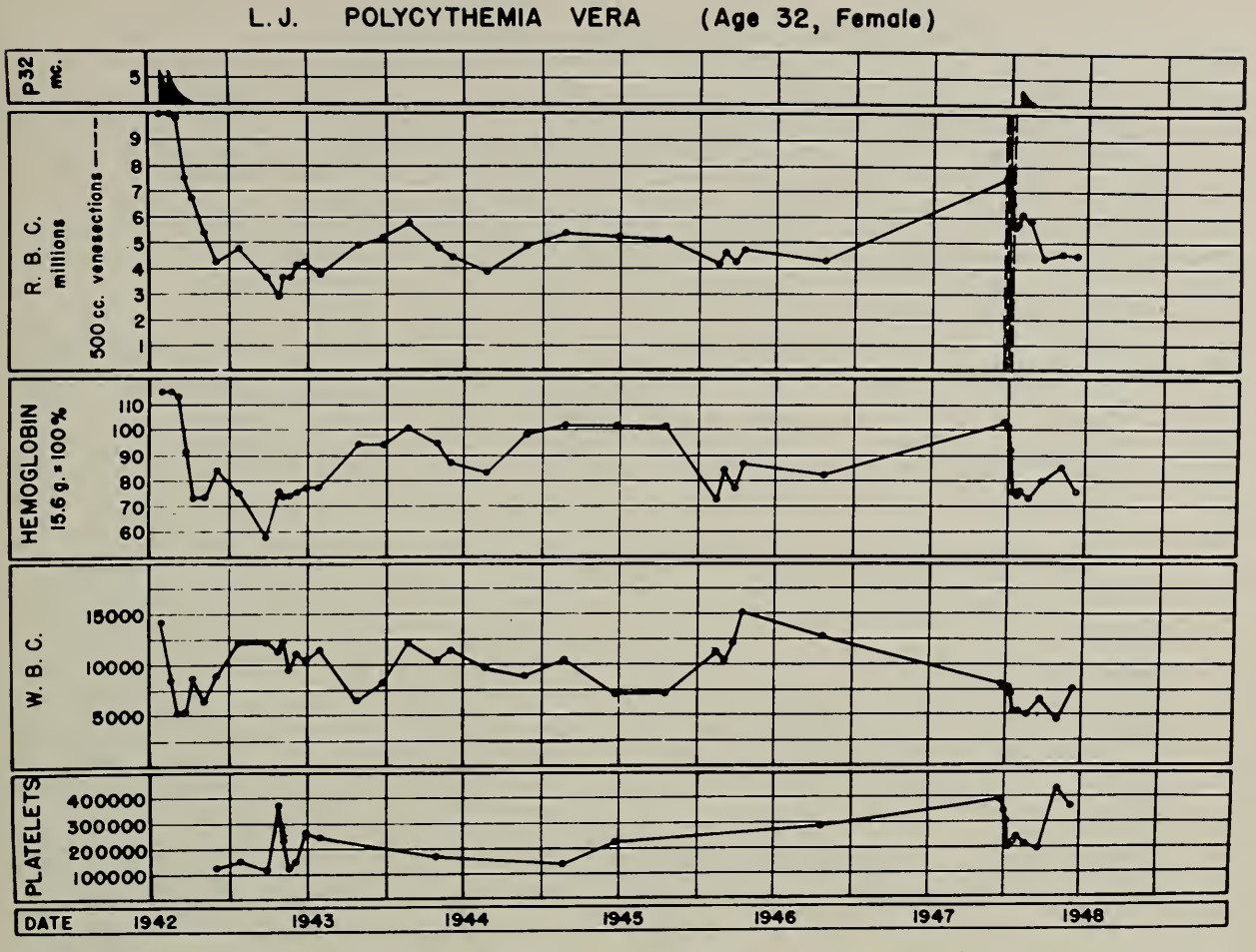


Figure 1.—This patient with classical polycythemia vera with enlarged spleen received 2 doses of P_{32} in 1942, resulting in a remission lasting over 5 years. Retreatment in 1948 has brought about another remission which continues.

giving these people a near normal life expectancy. It is of interest to point out that insulin is considered a control for diabetes, yet life expectancy in a recent large series reported by Lombard and Joslin[87] was only 10 years. Figures 1 and 2 are representative charts showing the hematological response to treatment.

For the treatment of chronic leukemia, both lymphatic and myelogenous, $_{15}P^{32}$ is at least as satisfactory in producing hematological and symptomatic remissions as x-ray and it now appears that it prolongs life somewhat longer[77, 79, 82]. There is another definite advantage of it over x-ray, namely, that the former practically never produces radiation sickness. In a series of over 300 patients with chronic leukemia, treated with $_{15}P^{32}$—beginning in 1936—the average duration of life after onset is approaching five years and this life duration is largely comfortable and useful. In this series over 30 per cent of the patients have lived over five years and some much longer. Figures 3, 4, and 5 are representative charts. Figure 6 is the chart of a young man suffering from polycythemia vera complicated by a leukemic blood picture. It is to be noted that the leukemic picture has been cleared up with P^{32}.

In none of these serious diseases has there been subsequently observed the induction of other tumors as a result of radiophosphorus therapy; yet several hundred patients have been treated and observed since 1936.

Complications of soluble $_{15}P^{32}$ therapy are leukopenia, thrombocytopenia, and anemia, and these constitute limiting factors in the dosage. In a few cases x-radiation has value in conjunction with $_{15}P^{32}$ therapy in reducing more rapidly the size of lymph nodes in lymphatic leukemia and in combating splenomegaly, particularly in myeloid leukemia. It has been common experience among workers concerned that therapy with $_{15}P^{32}$ requires a considerable degree of individualization. Its limitations in the form of the soluble phosphate for blood diseases are brought out in a recent article by Graff, Scott and Lawrence[41a].

$_{15}P^{32}$ in the treatment of skin lesions has been described by Low-Beer[88, 90]. He soaks a small piece of blotting paper in a labeled phosphate solution and applies this to the surface of the tumor or other skin lesion. The beta-rays from $_{15}P^{32}$ have a "half-penetration" of about 1 mm. in tissue, and this suggests $_{15}P^{32}$ may prove superior to x-ray or $_{88}Ra$ in the treatment of certain radiosensitive superficial skin lesions by avoiding irradiation of the deeper, uninvolved tissues.

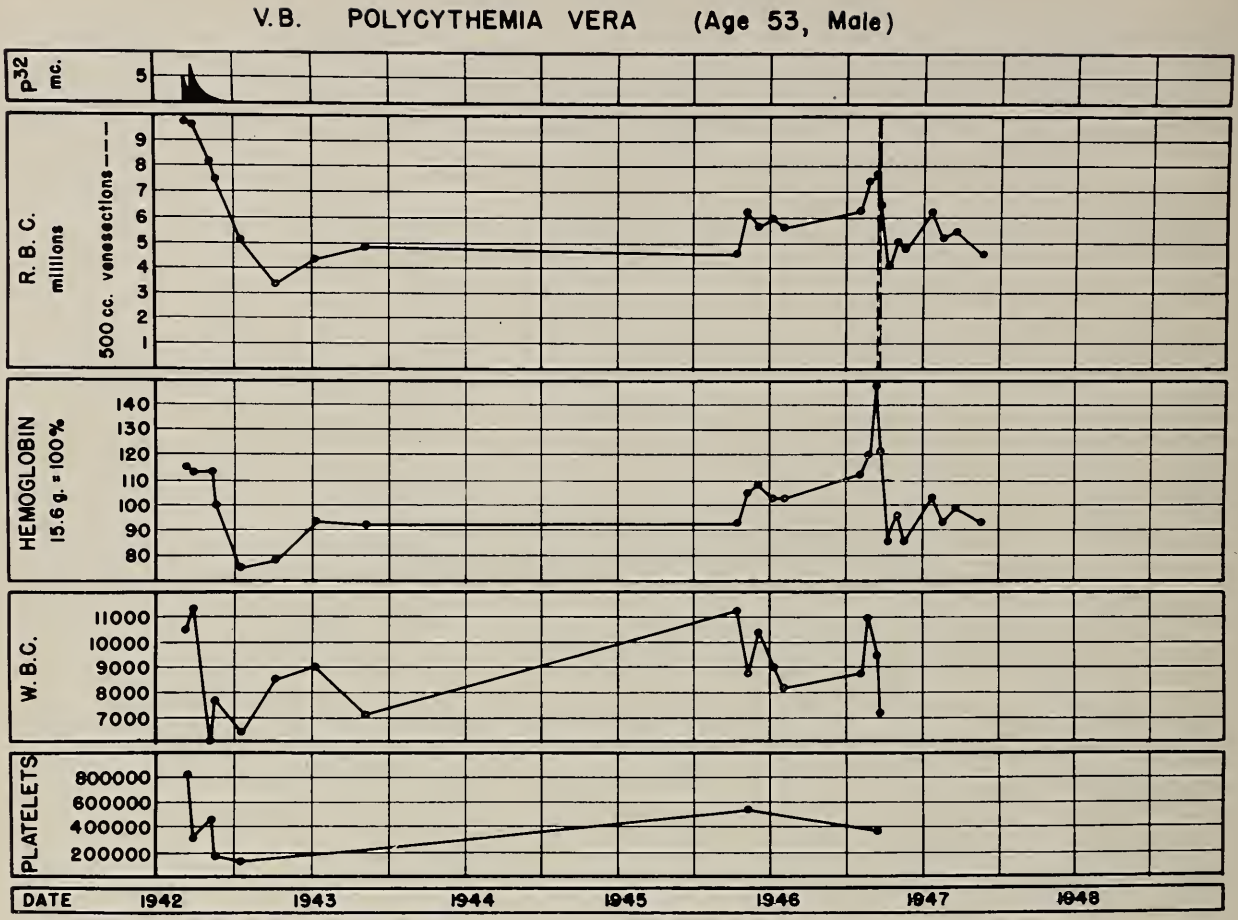


Figure 2.—Two injections of approximately 5 mc P_{32} in 1942 brought about hematological and clinical remission. In 1947, a moderate rise in the red cell level has been controlled by two venesections.

$_{15}P^{32}$ has also been used for experimental therapeutic purposes, in an insoluble colloid anhydrous chromic phosphate. Exploratory work during the past few years on the therapy of the splenomegaly and hepatomegaly of chronic leukemia and other diseases with this material has been carried on[67]. Another possible application of labeled chromic phosphate and colloids with similar properties is their use in the interstitial infiltration of chemically inert radioactive material into malignant growths. Allen *et al*[2] have injected chromic phosphate into the tissues around transplanted mouse tumors. They showed that the colloid remains at the point of injection and that the radioactive material can cause regression of mammary tumors under a certain size. Clinically this technique has recently been used for the injection of enlarged superficial lymph nodes in leukemia (Jones *et al.*[67]). It is possible that a similar procedure may prove of some value in the treatment of malignancies in inoperable sites.

The use of $_{15}P^{32}$ as a possible diagnostic tool has been suggested by Low-Beer and associates[89, 91]. They have found in a few cases that, if small doses of labeled Na_2HPO_4 are given to women with suspected breast carcinoma, the activity of the superficially located, malignant lesion (except for slowly growing mucoid carcinomata) is 25 per cent or more above that of the surrounding tissue of the skin. Benign lesions in their series showed less than 25 per cent greater activity. For such work the Strajman counter, a small mica-window Geiger-Müller counter that can measure gamma-rays and energetic beta-rays from *in vivo* sources (Strajman[133]), should have considerable value, particularly if localizing compounds emitting gamma-rays can be found.

$_{15}P^{32}$ has thus been shown to have considerable therapeutic value. Further research may well expand its clinical usefulness in the form of other inorganic or organic compounds, both in therapy and diagnosis.

Radioiodine ($_{53}I^{130}$ and $_{53}I^{131}$) in Therapy and Diagnosis:

The therapeutic use of radioactive iodine was reported upon for the first time simultaneously in 1942 by the Boston group[56] and the California group[52], for the treatment of hyperthyroidism (i.e., thyrotoxicosis, Grave's disease, Basedow's disease, etc.). Comprehensive reports on two series of patients with hyperthyroidism appeared in 1946, one by the former authors (Hertz and Roberts[58]) and the other by Chapman and Evans[14].

For therapeutic purposes carrier-free radioiodine in the form of an aqueous NaI solution is used, being administered by mouth. In the two most recent

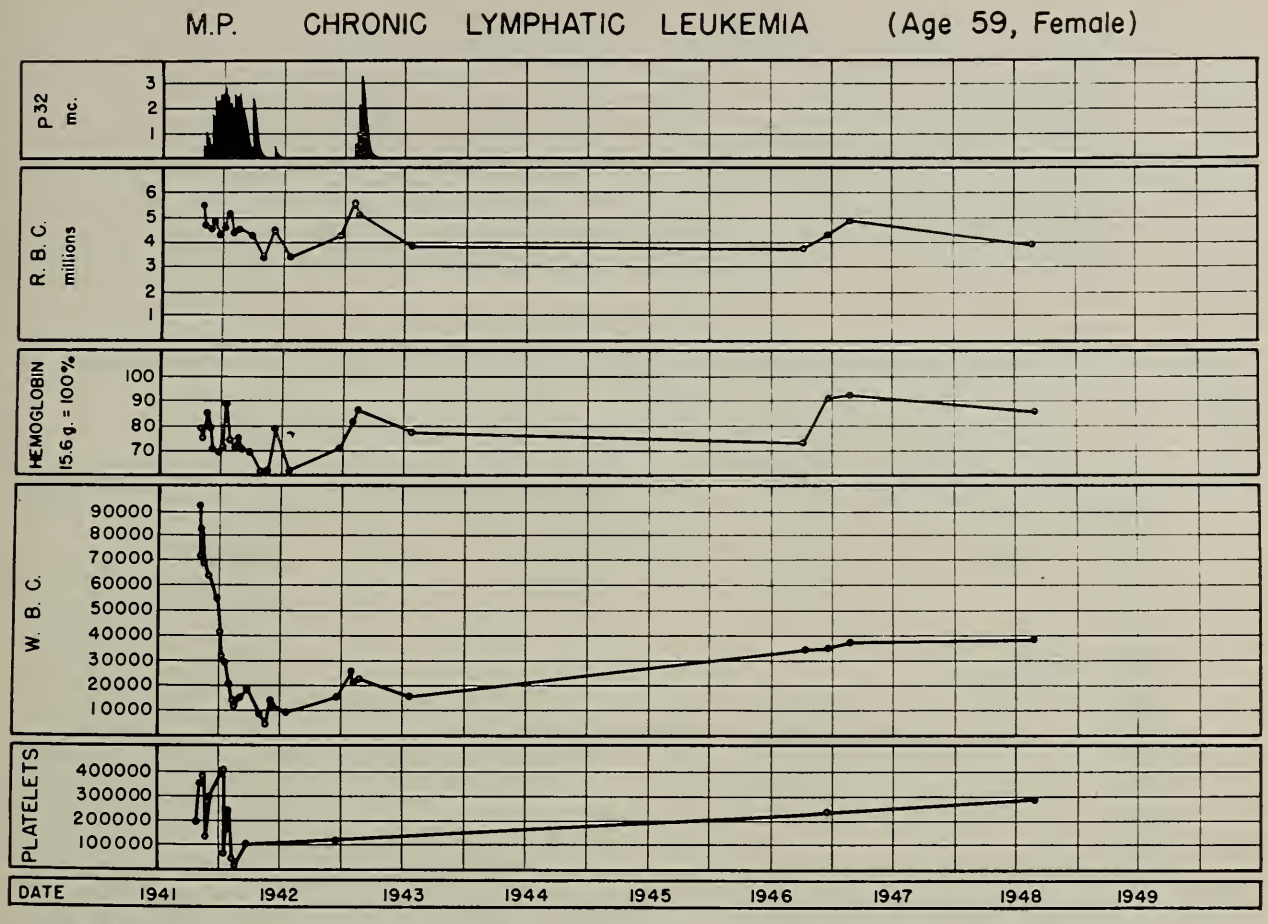


Figure 3.—Chronic lymphatic leukemia treated with multiple small doses of P_{32} in 1941 and 1942. There has been no treatment since then and the remission has lasted over six years.

papers, the iodine has consisted of a mixture of $_{53}I^{130}$ and $_{53}I^{131}$, of which the former has been the clinically more important component. The determination and calculation of dosage are given both by Hertz and Roberts and by Chapman and Evans.

Hertz and Roberts have found that about 80 per cent of their patients having thyroids of 60-75 gm. in size, and treated with an appropriate dose of radioiodine have been effectively cured. Chapman and Evans have also reported encouraging results. A complication of this form of therapy has been myxedema, resulting from an excessive depression of thyroid function, but as yet there have been no other post-irradiation effects such as the induction of carcinoma. The ultimate evaluation of this form of therapy as compared with other methods must await more extensive work and the passage of time.

In the last few years workers have also reported a few cases in which treatment of iodine-metabolizing thyroid malignancy has met with partial or considerable success when radioiodine has been used. Seidlin *et al.*[123, 124] have recently reported in detail on a case of metastatic thyroid adenocarcinoma in which metastatases took up iodine. This patient responded favorably to radioiodine therapy administered on three occasions—in March, 1943, April, 1944, and March, 1945. It would, therefore, appear that such treatment can be of value for those thyroid malignancies in which iodine is concentrated.

As a diagnostic tool for the determination of the level of the thyroid function, radioiodine appears to offer good clinical possibilities. So far most of the publications dealing with thyroid physiology as studied with radioiodine have been in the nature of fundamental investigations rather than of diagnostic developments. Hertz and Roberts[57], however, have shown that radioiodine can be used in distinguishing between simple hyperthyroidism and the ophthalmopathic type.

In general the use of radioiodine for the treatment and diagnosis of certain thyroid diseases appears highly promising.

Other Isotopes in Therapy and Diagnosis:

The use of isotopes of $_{11}Na$ and $_{38}Sr$ in therapy has been reported by various workers in the last few years. In addition, recent work with phosphate, $_{25}Mn$, $_{30}Zn$, $_{39}Y$, $_{40}Zr$, $_{41}Cb$, and $_{79}Au$ colloids shows promise.

Radiosodium $_{11}Na^{24}$ as labeled NaCl has been applied in the treatment of chronic leukemia by Thygesen, Vidaback, and Villaume[139] and by Lindgren[85]. The former workers observed favorable results in 7 cases of chronic lymphatic leukemia, but the report extended only over a period of 150 days. Lindgren.

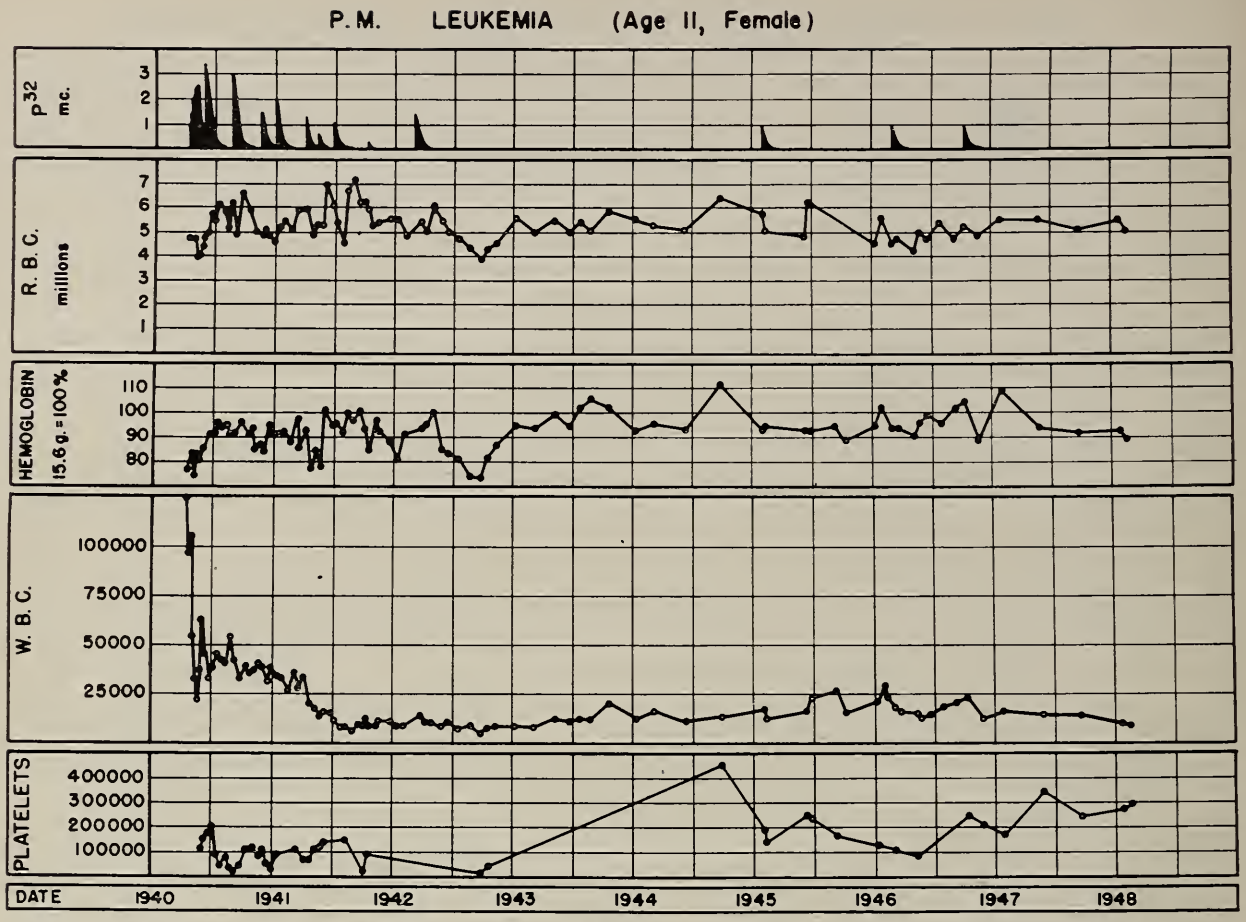


Figure 4.—Chronic myelogenous leukemia in a young girl treated in 1940, 1941, 1942, and in 1945 and 1946. The disease has been easy to control.

who treated five cases of leukemia with radiosodium and radiophosphorus, found that $_{15}P^{32}$ gave a much better response. A more recent paper by Evans and Quimby[31] on the effect of $_{11}Na^{24}$ on normal and leukemic mice suggests that this form of therapy may prove comparable to total body roentgen radiation. These workers found that the hematological response in normal animals was roughly the same with $_{11}Na^{24}$ as with equivalent roentgen irradiation. They did not, however, compare roentgen irradiation with $_{11}Na^{24}$ therapy in their leukemic animals, which appeared after administration of $_{11}Na^{24}$ to show a more rapid, although less prolonged, fall in the leukocyte count than did the normal. There are as yet insufficient published data for an evaluation of radiosodium therapy in chronic leukemia, but it is expected that the results would be similar to those following total body irradiation with x-rays, since there is for all practical purposes no selective localization of sodium.

The usefulness of $_{11}Na^{24}$ as a diagnostic tool is evident from a recent review by Quimby[111]. She has reported that in a number of circulatory diseases (arteriosclerosis, Raynaud's disease, etc.) and injuries (trench- and immersion-foot, frost-bite, etc.) of the extremities it has proved of considerable value in determining the status of the circulation. Since $_{11}Na^{24}$ can be measured by applying a Geiger-Müller counter to the surface of the skin and thus detecting its penetrating gamma-rays, its distribution in the blood and extracellular tissue fluids can be followed. With this technique of measuring tissue vascularity it has been possible to assist in evaluating the blood supply prior to amputation. Similar investigations with the radioactive inert gases are reported by Tobias, Lawrence and Hamilton[140].

The use of radiostrontium $_{38}Sr^{89}$ for the therapy of bone malignancies has been suggested on several occasions because of the concentration of this element in bone analogously with calcium. Its use was first suggested by the late Dr. Charles Pecher[108]. A comprehensive report on this material is still to be published. Actually, however, it is unlikely that diffuse irradiation of bone and marrow for relatively localized malignant growths will prove of much value, particularly in view of the danger of marrow depression. Nevertheless beneficial results have been obtained in the treatment of metastatic prostate cancer in the way of slowing down of the malignant process and control of pain (Lawrence[74]).

A number of radioactive colloids have been used in preliminary therapeutic studies. These include, as already mentioned, anhydrous chromic phosphate, which localizes almost entirely in the liver and spleen[67]; colloidal MnO_2 protected by gelatin[48, 126]; zinc suspended in a suitably prepared solution of

pectin[102]; colloids of several elements, radioisotopes of which occur as fission products ($_{39}$Y, $_{40}$Zr, and $_{41}$Cb)[22, 23, 68]; and colloidal sols of gold[46a, 125a]. The fission colloids may, depending upon the method of preparation, concentrate almost exclusively in the liver and spleen or go in equal concentration into the bone marrow[22, 68]. Because of the relative abundance of $_{39}$Y, $_{40}$Zr, and $_{41}$Cb in fission, there is a potentially rich source of their radioactive species for such investigations and for possible widespread clinical application. Investigations with radiomanganese as labeled colloidal manganese dioxide in an aqueous medium with gelatin as a protective colloid have recently been reported by Hahn and Sheppard[48, 126]. These authors suggest the possibility that this material may be localized upon intravenous injection in the lymphoid reticuloendothelium. More recently Sheppard, Goodell, and Hahn[125a] have suggested the use of gold sols labeled with $_{79}$Au[198] for this purpose.

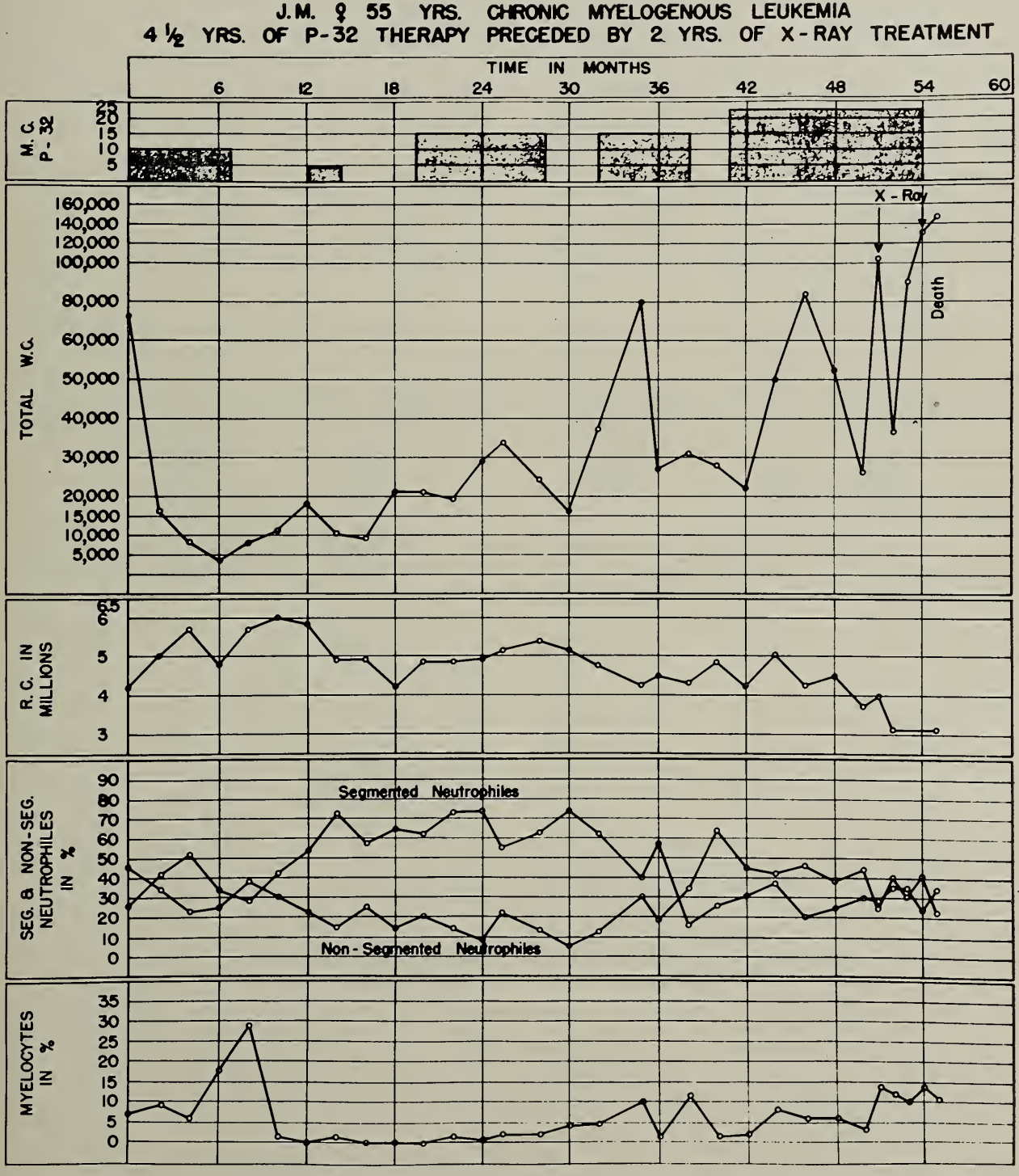


Figure 5.—Chronic myelogenous leukemia. Satisfactory response to therapy for four years, then failure to respond to further treatment.

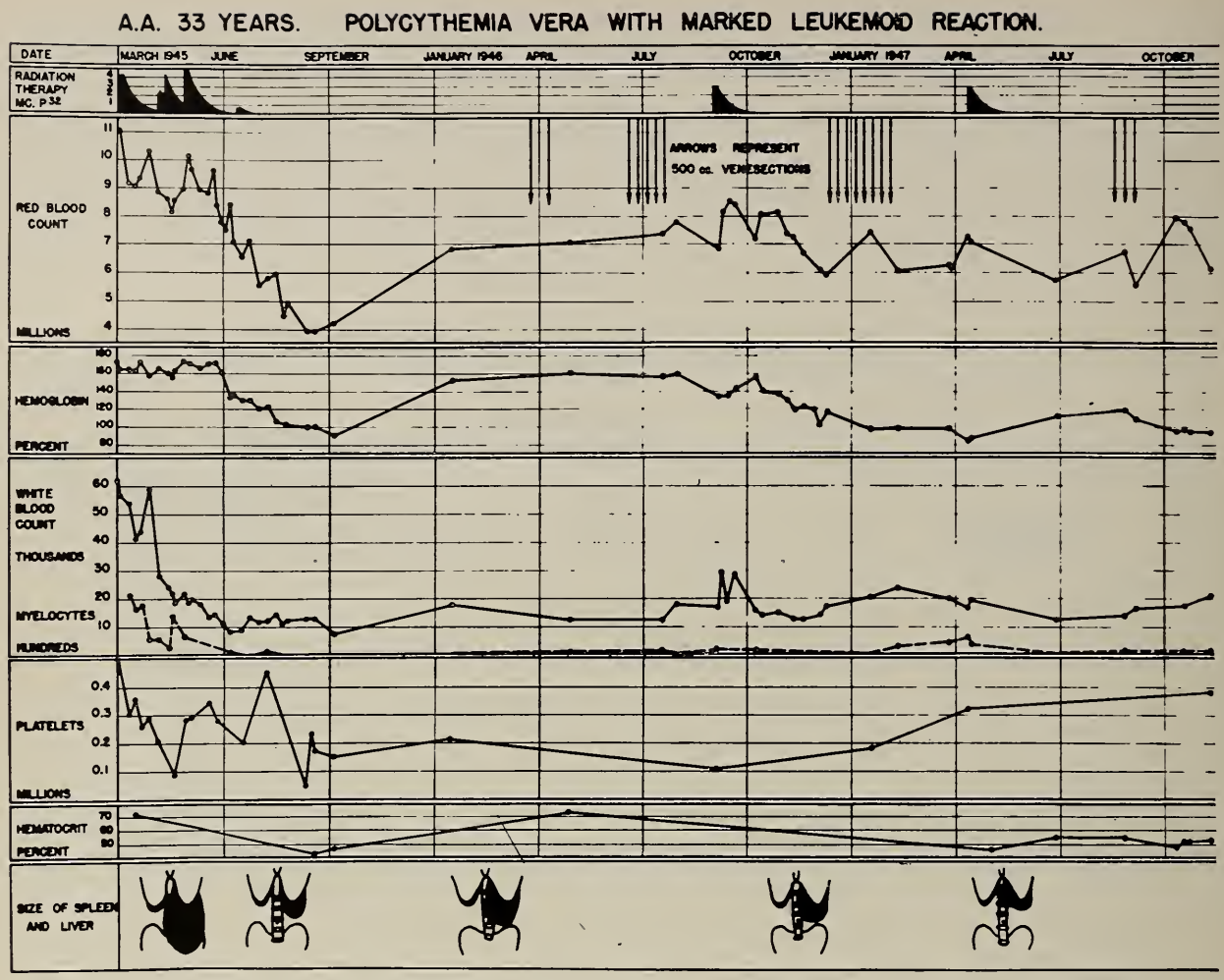


Figure 6.—Polycythemia vera with leukemic blood picture prior to treatment with P_{32}. The elevated red blood cell count has been controlled with some difficulty, but the leukemic blood picture has been suppressed up to the present time (June 1948). The patient has been relatively symptom-free during this three-year period.

In addition to the intravascular use of these colloids there are also, as mentioned, possible applications in interstitial infiltration of malignant growths, (Allen *et al.*[2]). Müller[102] has recently reported on the use of $_{30}Zn^{63}$, a short-lived isotope of 38.3 minutes half-life, in the interstitial injection of uterine carcinomata (2 cases) in a pectin-protected suspension of $_{30}Zn$; he reports the strict localization of the isotope in the region of inoculation during the period of its effective activity and a tissue reaction similar to that following $_{88}Ra$ therapy. Hahn *et al.*[16a] have given encouraging accounts of the clinical applications of gold sols containing $_{79}Au^{198}$ and given interstitially and intraperitoneally in the treatment of certain malignant growths. In general the use of labeled colloidal materials is promising and deserves thorough clinical trial. It is a step in the direction of selective irradiation therapy.

Although $_{15}P$ and $_{53}I$ radioisotopes are the only artificial species for which therapeutic applications have been proven, it seems quite likely that in a few years a number of different isotopes will have well accepted clinical uses. In addition to the elements already mentioned there are important possibilities in the labeling of organic compounds with long-lived radiocarbon—$_6C^{14}$—and radiohydrogen or tritium—$_1H^3$ or T. If radiation is ever to prove a vital tool for the palliation or cure of malignancy, the only possible way to accomplish this end would seem, from our present perspective, to be the discovery of organic substances which undergo highly selective localization in various types of cancer cells in contrast to those of normal tissue and which can be labeled with a suitable radioisotope. T, with the low penetrating power of beta-rays and its rapid turnover in the body, is particularly interesting in this regard. If it can be put in relatively stable positions in localizing compounds, it will expend most of its ionizing power within the concentrating cells. Potentially it is an ideal radiotherapeutic agent.

A discussion of radiotherapy with isotopes would not be complete without mention of fissionable isotopes—i.e., of uranium—$_{92}U^{235}$—and plutonium—$_{94}Pu^{239}$—and of other isotopes that release large amounts of ionizing radiation upon being bombarded with slow neutrons—i.e., of lithium—$_3Li^6$—and boron—$_5B^{10}$. If these materials can be localized in given tissues and organs and the region bombarded with slow neutrons, a significantly higher radiation can be conferred on the isotope-containing

tissue than on the normal or uninvolved tissue through which the neutrons also must pass. Kruger[73] has shown that pieces of transplantable mouse tumor soaked in boric acid solution and then irradiated *in vitro* with slow neutrons before inoculation into new hosts showed a significantly lower percentage of "takes" than control tumor pieces soaked in boric acid but not irradiated. Zahl, Cooper, and Dunning[153] have shown that, if $_3$Li or $_5$B salts are infiltrated into mouse tumors *in vivo* and the host animals bombarded with slow neutrons, there is a significant increase in tumor regression over that in bombarded, but uninjected controls. Recent work of Tobias, Weymouth, Wasserman, and Stapleton[142] on the effect of colloidal UO_2 enriched with $_{92}U^{235}$ concentrated in the liver and spleen of mice and there subjected to slow neutron bombardment also clearly shows the enhanced effect of radiations when nuclear disintegration processes of high energy are induced in tissues. It is interesting to note that these workers observed a greater biological effect per unit of tissue ionization with fission recoils than with beta particles. There seems little chance, however, that such studies will ever lead to therapeutic applications because of the short mean free path of thermal neutrons, the damaging effects of the infiltrating neutrons, and the toxic effects of fissionable materials.

Finally there should be mentioned the possible therapeutic use of charged nuclear particles—protons (p), deuterons (d), and alpha particles (α)—of high energies from the cyclotron and other heavy particle accelerators. This would be an isotopic application of sorts inasmuch as the nuclei of single species of hydrogen ($_1$H) and helium ($_2$He) are being employed. None of these has been used clinically as yet. But recently Wilson[150] has suggested the possibility that very high energy protons—of 100 Mev or more—produced by the giant cyclotrons might find use in direct beam radiotherapy. The 100 Mev proton would produce its maximum ionization some centimeters beneath the skin and thus might be used to radiate deep-lying lesions, especially where the skin tolerance is a limiting factor. A comparable, although non-istopic, application of accelerated particles might be the use of high energy electrons from the betatron as suggested by Kerst[71] and Quastler[110]. Also deuterons may be used to produce fast neutrons from beryllium ($_4$Be); these and other neutrons have been used in a number of studies on the biological effects of irradiation (Aebersold and Lawrence[1]; Stone and Larkin[132]).

In summary it may be observed that the role in therapy of radioactive isotopes and of those stable species that can also be adapted to the production of ionization in tissues is still in a primitive stage of development. Unquestionably, the future will see great expansion in our knowledge of their usefulness and practical application. The use of the new types of radioactivity must, however, be approached with caution. It has long been known that ionizing radiation in addition to its acute effects may have such chronic manifestation as the induction of malignant change in tissue. Radium-induced bone sarcomata have been observed for many years. Recently Lisco, Finkel, and Brues[86] have shown that both radiostrontium—$_{38}Sr^{89}$—and plutonium—$_{94}Pu^{239}$—can produce bone tumors in mice, particularly the former. This has particular significance for the possible use in man of long-lived isotopes of elements that concentrate in bone—as for example, many of the fission product elements.

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California Cancer Commission Studies*

Chapters XIX and XX

Carcinoma of the Stomach

H. Glenn Bell, M.D., *San Francisco*

THE yearly deaths from carcinoma of the stomach number approximately 45,000. It is estimated that 10,000 of the patients who die might be saved if they were operated upon early. Treatment by x-ray and radium is of no value. *Cancer of the stomach cannot be cured except by removal of the growth.*

Cures of cancer of the stomach will increase only with its earlier recognition. Its onset is insidious, usually with few symptoms, and there is no single group of symptoms which is absolutely characteristic. Certainly *any person 35 years of age or over who has indigestion of more than one week's duration should be suspected of having carcinoma of the stomach.* A short history of indigestion in an older man is an alarming symptom, even without a palpable mass. Symptoms of obstruction may indicate a tumor occurring at the outlet of the stomach. Chronic indigestion, loss of weight or strength or both, or vomiting of blood or any material that looks like blood, indicate the need for careful investigation. Do not wait for the appearance of these symptoms before investigation, because some of them may indicate already advanced disease.

When carcinoma of the stomach is suspected, it is up to the doctor, with the cooperation of the patient, to do everything possible to prove or disprove this diagnosis. A careful physical examination must always be done. This should include a rectal examination, since one of the first findings in carcinomas of some types is a so-called rectal shelf—which, however, indicates incurable disease.

A careful x-ray examination, particularly fluoroscopic examination, should be done by a qualified radiologist to determine the possibility of a filling defect, or an irregularity or rigidity of a portion of the stomach. It should be stressed that *if the roentgen examination is negative, a patient with continued symptoms referable to his stomach should have a repeat examination after a period of two weeks*, regardless of whether or not he is on any sort of special diet.

A routine blood count is important. Many patients with indigestion have a moderate to severe secondary anemia. Too many are treated for an indefinite period for an unexplained secondary anemia. *Any unexplained secondary anemia means either carcinoma of the stomach or carcinoma of the right colon until this is absolutely disproved.* A gastric analysis is informative, as an achlorhydria would point toward, but not necessarily clinch, the presence of cancer of the stomach. Achlorhydria is found in 60 per cent of patients with carcinoma of the stomach.

Every patient with pernicious anemia should have a fluoroscopic examination of the stomach yearly, since approximately 8 per cent of these patients develop cancer.

Gastroscopy, *in competent hands*, may be of value in differential diagnosis.

Too often doctors tell their patients that nothing can be done for cancer of the stomach. This pessimistic attitude is all wrong. Necropsy data show that over 20 per cent of persons dying of cancer of the stomach have a lesion which is still confined to the stomach. *An exploratory operation should be done in every case of cancer of the stomach unless distant metastases are unequivocally demonstrated.* A resectable lesion is frequently found at operation, even though preoperative examination reveals a large, bulky tumor palpable in the upper abdomen, a large filling defect shown by x-ray, achlorhydria and secondary anemia. Some of these patients live well beyond the five-year survival period. *The surgeon must always be prepared to do an extensive and drastic procedure.* (Plate I.) What is inoperable in the hands of an inexperienced surgeon may be resectable in other hands. In some cases even when there is metastasis, a palliative operation may afford the patient relief for a considerable time. The operative technique and preoperative and postoperative care of these patients have been developed to a very high degree. Subtotal or total resection of the stomach for carcinoma should be carried out with a mortality rate of 10 to 15 per cent, or less in special clinics.

It is known, of course, that the five-year survival rate in all cases of cancer of the stomach is very low (10 to 15 per cent). A tumor occurring at the outlet of the stomach may cause symptoms of obstruction leading to an early diagnosis, and for this group the five-year survival rate is higher (18 per cent). Doctors in general should keep in mind that the only way to increase the survival rate for carcinoma of the stomach is to make the diagnosis *early* while the lesion is still localized in the stomach. Livingston and Pack as well as Walters, Gray and Priestley have shown that if gastric resection can be done when the carcinoma of the stomach is entirely confined to that organ the five-year survival rate reaches 55 per cent.

*Organized by the Editorial Committee of the California Cancer Commission.

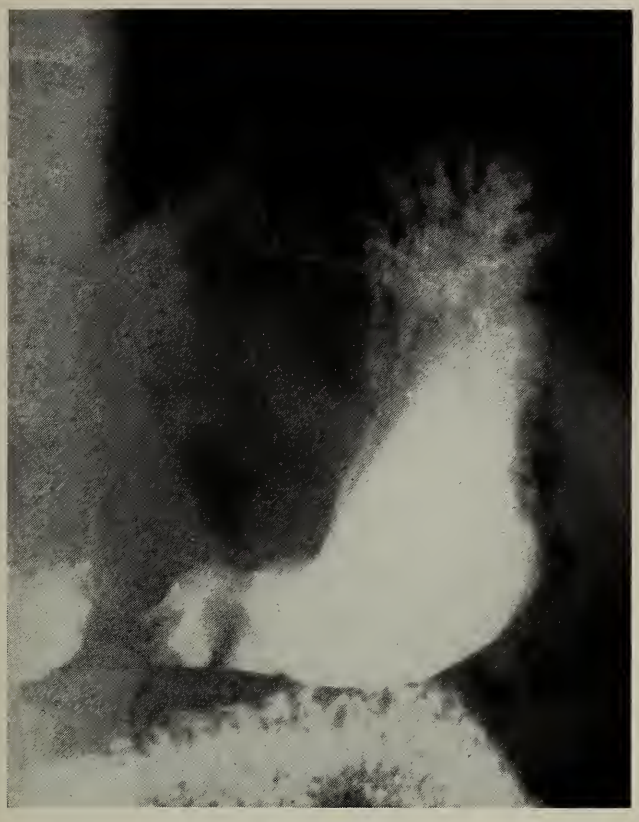


Figure 1.—Roentgenogram of 56-year-old man with history of ulcer for two years. Films were read as showing a prepyloric ulcer. Medical treatment prescribed. 1941.

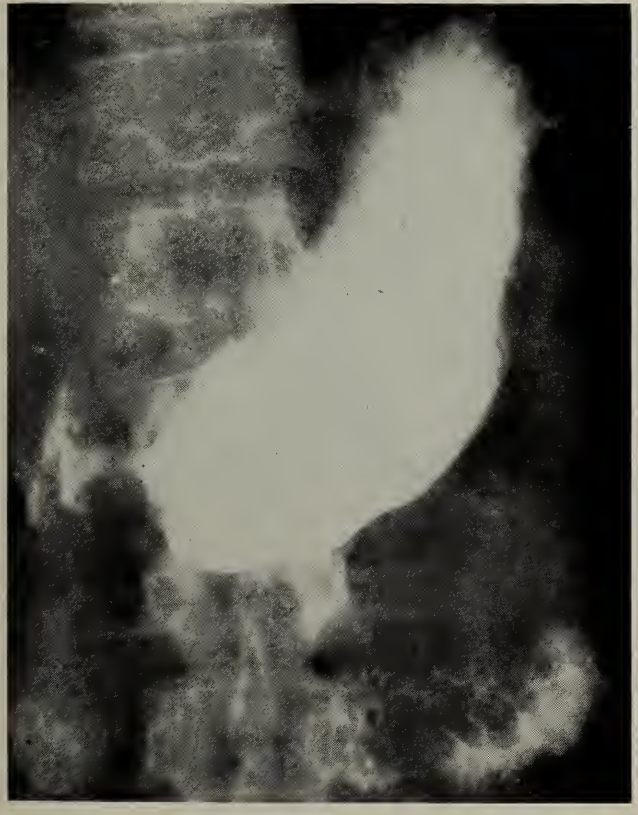


Figure 2.—Same patient as in Figure 1, 1943. Medical treatment continued.

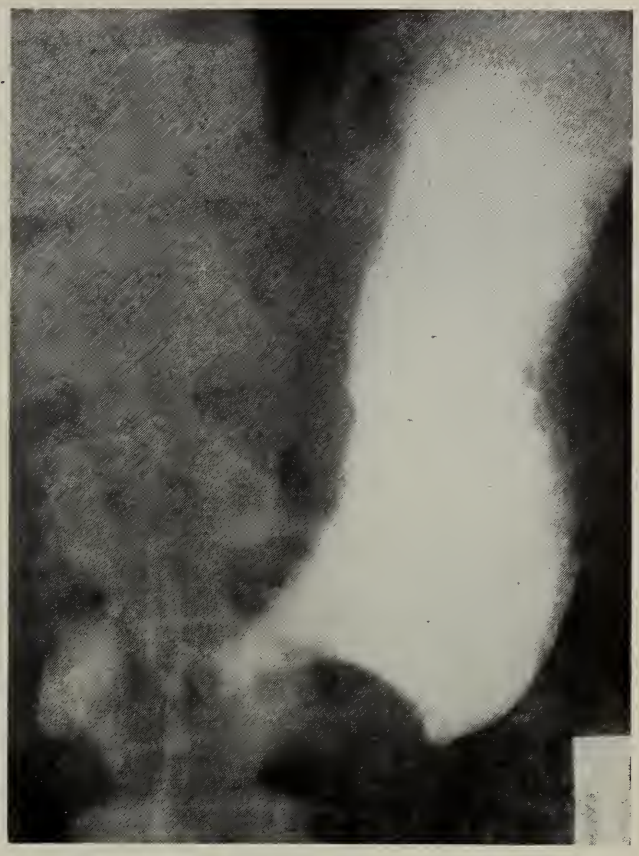


Figure 3.—Same patient as Figure 1 and 2, 1946. Radiologist, patient, and patient's physician all agreed that he now had cancer of the stomach. How much better if surgery had been done in 1941 or 1943, instead of 1946!

The relationship of ulcers of the stomach to carcinoma is a question that frequently arises. Any gastric ulcer is liable to suspicion until proved benign. We know that some carcinomatous ulcers of the stomach will show evidence of healing on a medical regimen (See Figures 1, 2, 3). Any gastric ulcer that does not improve markedly and practically disappear in two weeks under medical treatment should be operated upon and a subtotal gastric resection done with removal of one-half to three-fourths of the stomach, giving the ulcer a very wide margin. About 18 to 20 per cent of gastric ulcers which are thought to be "benign" are found, on microscopic examination, to be carcinoma. The five-year survival rate in these cases is 40 to 60 per cent.

Other gastric tumors that might be considered are lymphosarcoma, leiomyoma, and polyps. Polyps in the stomach are definitely precancerous lesions; therefore, they should be removed either by local excision or by subtotal gastric resection. The leiomyomas are not usually malignant, but may undergo malignant changes; while they are not usually diagnosed preoperatively, any tumor in the stomach should be removed surgically if possible. Lymphosarcoma of the stomach, if localized, should be removed surgically. Again the tumor is not usually diagnosed specifically before operation. Lymphosarcoma does respond, at least for a period of time, to x-ray therapy; so if there is an extensive involvement

of the stomach with regional spread, a biopsy should be taken to prove the diagnosis but no further surgery should be done. The patient should then be sent to a competent radiologist for radiation therapy.

SUMMARY

Cancer of the stomach is a frequent malignant lesion. Any persistent indigestion in an individual over 35 years of age—particularly a male, as cancer is more frequent in males than in females—indicates the need for a physical examination and x-ray and laboratory studies either to demonstrate or rule out a carcinoma of the stomach. The only treatment for carcinoma of the stomach is complete excision of the tumor with a wide margin of normal tissue. *The only hope for increasing the number of cures of carcinoma of the stomach is the earlier recognition and earlier surgical treatment of this disease.* The pessimism of so many doctors is wrong. It causes delay and destroys the only chance of a cure by early operation.

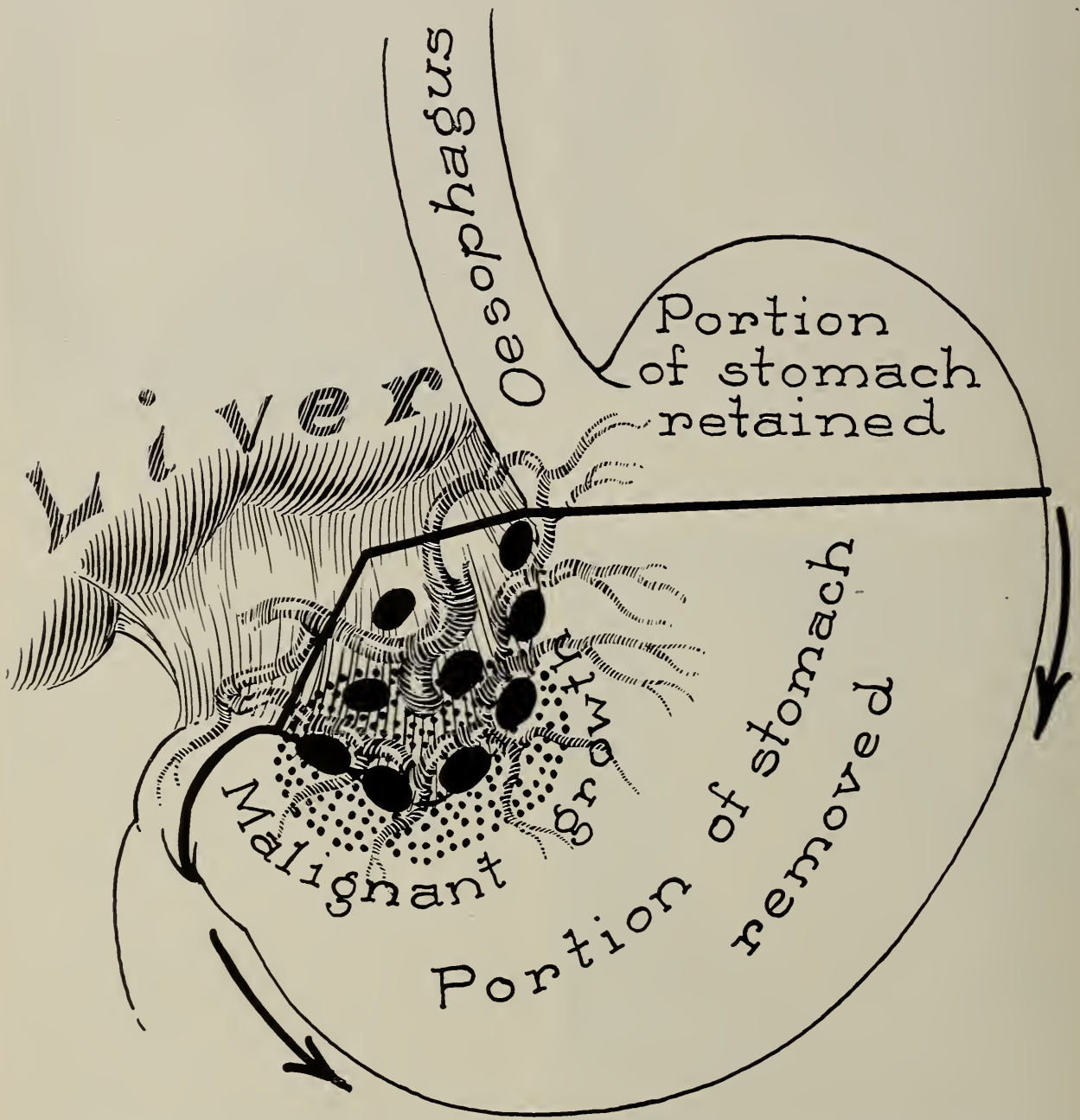


Plate I.—Showing the amount of stomach which should be removed for the ordinary carcinoma of the stomach. In carcinoma higher up, a total resection should be done. The entire lesser curvature and lesser omentum, as well as the greater omentum, should be removed.

Carcinoma of the Colon

Robert A. Scarborough, M.D., *San Francisco*

THERE are approximately 30,000 deaths in the United States each year from carcinoma of the colon and rectum. These comprise 17 per cent of all deaths due to cancer. Nevertheless, the possibility of permanent cure is greater for cancer of the large bowel than for cancer anywhere else within the body. In many of the larger clinics the resectability rate is now between 80 and 90 per cent, the operative mortality is well below 10 per cent, and the five-year nonrecurrence rate is better than 50 per cent. This represents five-year "cure" in about one out of every three patients. During the past 15 years considerable progress has been made in surgical technique, in anesthesia, and in preoperative and postoperative care. Yet during the same period of time there has been no appreciable lessening of the time interval between the onset of symptoms and the establishment of diagnosis. This interval continues to average between eight and nine months. *Curability is directly related to early diagnosis. The opportunity for early diagnosis belongs largely to the general practitioner* who is first consulted for symptoms which are seldom pathognomonic of large bowel neoplasm, but which should always create suspicion of such disease.

SYMPTOMATOLOGY

There are no pathognomonic symptoms upon which to base an early diagnosis of carcinoma of the colon. However, there are usually symptoms which direct attention to the bowel and demand careful investigation.

Right Colon: Primary function of this portion of the colon is absorptive. The lumen of the bowel there has its greatest diameter and the contents of it are liquid. Symptoms, therefore, are primarily the result of physiologic disturbance, and obstructive symptoms are uncommon. Tumors in this area are usually large, cellular, and ulcerated. Toxic products are readily absorbed, producing *constitutional symptoms of anemia, weight loss, and fatigue.* Abdominal distress of some kind is usually present. There may be a sensation of fullness, of weight, or of tightness in the right side of the abdomen. Cramps or indefinitely localized pain may occur. Not infrequently the patient himself has discovered a palpable mass. Fewer than half of the patients will have had any noticeable change in bowel habits. Mild diarrhea is twice as common as increasing constipation. Only 10 to 20 per cent have gross blood in the stools.

Left Colon: Primary function here is storage. Constitutional symptoms are conspicuously lacking. Any marked anemia or weight loss is suggestive of metastases. The patients frequently exhibit an appearance of vitality and well-being which belies the serious nature of the disease responsible for the apparently minor symptoms for which the doctor is often apologetically consulted. The dominant symptoms are *change in bowel habits and bleeding.* Most frequently there is increasing constipation, with minor abdominal cramps and variable distention. About one-third of the patients describe an increased frequency of stools. Less commonly there is a true diarrhea, with numerous watery stools daily. Alternating constipation and diarrhea does occur, but in only a small percentage of patients. Occasionally there is a sudden initial onset of complete obstruction with no prodromal symptoms. Blood in the stools is noted by about 50 per cent of patients. This may consist of only occasional streaks of bright red blood, or there may be larger amounts of bright or dark red blood sometimes with the passage of clots. Episodes of severe gross hemorrhage may occur.

DIAGNOSIS

Evidence of weight loss and anemia may be observed in patients with carcinoma of the proximal colon. A palpable tumor may be present. These signs are rarely evident in lesions of the distal colon until a late stage in the disease. Abdominal distention may be present in lesions of the descending colon and sigmoid, but seldom is this evident in the early stages. The liver edge should always be palpated carefully for evidence of metastases. Localized signs of peritoneal irritation, simulating appendicitis or diverticulitis, may be present when the lesion is complicated by penetrating infection. Secondary abscess formation may occur, with classical symptoms and signs which entirely overshadow the underlying neoplasm.

Digital examination of the rectum is of greatest importance in diagnosis of carcinoma of the rectum. Furthermore, some tumors of the sigmoid, too high up to be directly palpated through the lumen of the bowel, may be felt through the rectal wall in the cul-de-sac, into which the tumor may have gravitated by its own weight. Occasionally such a lesion, still resectable, is thought to be due to peritoneal implants in the cul-de-sac and considered inoperable.

Sigmoidoscopic examination is of great value, not only for direct visualization of tumors of the rectum and lower sigmoid, but to rule out non-malignant ulcerative disease, and at times to verify the fact that blood is actually coming from higher up in the colon.

The actual diagnosis of lesions beyond reach of the sigmoidoscope depends largely upon x-ray examination by barium enema. It should be emphasized that such examination, even with the best technique, has a diagnostic accuracy of only about 90 per cent. Even large carcinomas are not always demonstrated, especially in the region of the colon flexures, or where redundant loops of sigmoid mask the critical area. *A second and even third examination is indicated when the clinical evidence points toward a diagnosis of carcinoma.* Instances do occur in which the diagnosis is made only by exploratory laparotomy after repeated negative x-ray findings. The criteria for x-ray diagnosis include persistent obstruction to the flow of barium in spite of manipulation and change of position of the patient, or a persistent filling defect

which may be annular or polypoid. The introduction of air or oxygen into the colon after evacuation of the barium enema is of particular value in the demonstration of polypoid lesions.

A "gastro-intestinal series," in the meaning of the term as it is commonly used, actually is only diagnostic of lesions in the stomach and duodenum. The colon is not visualized in sucient detail to permit the diagnosis of intrinsic lesions. Satisfactory examinaton of the colon demands barium enema examination.

Stool examinations are useful to rule out parasitic disease. The presence of parasites, however, does not necessarily rule out malignancy. The presence of occult blood in the stool deserves every consideration as a sign of suspicion, but is not necessarily pathognomonic of neoplasm. The presence of gross or occult blood in the stool does make it mandatory that cancer be thoroughly searched for.

DIFFERENTIAL DIAGNOSIS

Right Colon: Symptoms may simulate those of peptic ulcer, carcinoma of the stomach, cholecystitis, and tumors or inflammatory lesions of the kidney. Tuberculosis and regional colitis may produce symptoms and roentgenologic signs similar to those of carcinoma. In the case of carcinoma, barium enema examination usually shows a relatively shorter segment of bowel involvement, with a more sharply delineated filling defect. In tuberculosis there is usually an active pulmonary lesion. Amebic granuloma, though rare, may closely simulate carcinoma. Appendicitis, and particularly appendiceal abscess, may be easily confused with carcinoma of the cecum. Differentiation by x-ray examination is usually but not always possible.

Carcinoma of the proximal colon ranks in importance with carcinoma of the stomach as a cause of secondary anemia. A diagnosis of unexplained secondary anemia without x-ray examination of the stomach and colon is fraught with tragedy.

Left Colon: Differentiation of diverticulitis and carcinoma is a recurring and oftentimes difficult problem. Carcinoma complicated by inflammation or abscess formation may produce the classical symptoms and signs of diverticulitis with pain, fever, leukocytosis, and localized signs of peritoneal irritation. Diverticulitis may produce obstructive symptoms and in some instances bleeding, with none of the signs or symptoms of inflammatory disease. Differentiation by barium enema examination is often difficult, sometimes impossible. Comparative studies of numerous films are of the greatest value. The filling defect of a carcinoma tends to remain constant, while the narrowing and irregularity due to diverticulitis are less constant, with some variability in the diameter of the lumen and the contour of the defect. Diverticulitis may produce an inflammatory tumor which is not only indistinguishable from carcinoma by x-ray examination but may be so even on surgical exploration. A carcinoma may at times be entirely overshadowed by deformities due to diverticulosis and diverticulitis. Although bleeding does occur at times in diverticular disease, this symptom should always suggest the possibility of coexisting carcinoma.

A diagnosis of chronic ulcerative colitis as the explanation of symptoms of diarrhea and bleeding is never justified without confirmation of the actual existence of the disease by proctoscopic examination.

Irritable colon, with symptoms of bowel irregularity, requires differentiation by x-ray examination. Segmental spasm may simulate the filling defect of carcinoma, but the defect tends to be inconstant in repeated films.

Fecal impactions may produce obstructive symptoms or extreme diarrhea. Their presence may result in apparent filling defects on x-ray examination. Digital examination of the rectum will immediately determine the presence of rectal impaction. After the elimination of all impacted stool there may be spectacular cessation of symptoms, and apparent filling defects may entirely disappear on repeat x-ray examination.

Pelvic tumors of inflammatory or neoplastic origin may compress the sigmoid, producing symptoms referable to the bowel. Endometrioma may involve the wall of the bowel and may cause rectal bleeding. The majority of such lesions occur at a level which can be reached with a sigmoidoscope. Visualization of an intact mucosa at the site of such a tumor should prevent a mistaken diagnosis of carcinoma of the bowel.

One should not be misled by the presence of hemorrhoids. When there is bright red blood in the stool one must always rule out cancer of the colon first.

TREATMENT

There is but one curative treatment for carcinoma of the colon, and that is radical surgical excision of the involved segment of bowel together with wide removal of the corresponding area of lymphatic drainage and regional lymph nodes. Successful operation depends largely upon the technical skill of the surgeon. A thorough understanding of the problems of blood supply to the colon is imperative. Much depends upon the judgment of the surgeon in the proper choice of the best method of surgical treatment to be used in each individual case. There are proper places for single stage and multiple stage operations, for primary anastomosis by an open or closed method, for end-to-end or side-to-side or end-to-side anastomosis and for obstructive resection based upon the Mikulicz procedure.

Adequate preoperative preparation is of the greatest importance, including measures for mechanical decompression of the colon, correction of vitamin and protein deficiencies, transfusion, and attention to control of any coexisting disease. The use of sulfasuxidine and sulfathalidine is a valuable adjunct to preoperative preparation. It should be recognized, however, that these drugs by no means eliminate any of the possible complications of surgical operation, and that their use permits no relaxation of the principles or precautions necessary for success.

Postoperative care is directed toward the avoidance and control of potential complications and toward early restoration of adequate nutrition.

Due consideration should be given to the psychological problems which are incurred by the patient with cancer. Optimism and assurance are justifiable on the basis of the relatively high possibilities of cure. Following recovery from successful surgical extirpation, repeated reassurance is frequently necessary for the peace of mind and physical welfare of the patient. Minor subjective complaints, or the development of symptoms of entirely unrelated illness may convince the patient that he is hopelessly riddled with cancer. This incorrect assumption is occasionally made by the doctor. While such a possibility must necessarily be kept in mind by the physician, acceptance of the fact should never precede the establishment of definite evidence that metastases are present.

The recurrence of symptoms of bowel irregularity or of bleeding are not presumptive evidence of recurrence of cancer. The incidence of development of new primary lesions is sufficiently high to suggest this possibility. In such an event, the prognosis for cure by surgical excision of the new lesion is equally as favorable as it was for the first lesion.

SUMMARY

1. Carcinoma of the colon and rectum is responsible for 17 per cent of all deaths due to cancer.
2. The possibility of cure is greater for cancer of the large bowel than for cancer anywhere else *within* the body.
3. Curability is directly related to early diagnosis.
4. There are no pathognomonic symptoms upon which to base an early diagnosis. However, unexplained secondary anemia, change in bowel habits, or blood in stools demands careful investigation of the large bowel.
5. A complete physical examination should be done. In addition a digital palpation of the rectum, sigmoidoscopic inspection and x-ray examinations with barium enema are necessary.
6. The one curative treatment is radical surgical excision.

POLYPS OF THE COLON

The colon and rectum are a frequent site for the development of polyps. There is abundant evidence that the vast majority of these tumors are precancerous lesions. Their discovery and destruction will prevent carcinoma in many instances. Polyps may develop at any age. They are the commonest cause of intestinal bleeding in children. Probably 4 per cent of adults harbor one polyp or more in the large bowel. They may occur singly, or there may be a few or great numbers. Multiple polyposis is frequently but not always a familial disease. About 10 per cent of patients with chronic ulcerative colitis develop multiple polyps, a condition which has been called pseudopolyposis because of the inflammatory origin of the lesions. These, too, are precancerous lesions.

Polyps produce no symptoms until surface ulceration results in bleeding or until there is mechanical interference with bowel motility. By far the commonest symptom is bleeding. There may be gross hemorrhage, but in the vast majority of cases the only symptom is streaking of blood on the stool.

Diagnosis is achieved by sigmoidoscopic examination of the lesions within reach with this instrument. Higher lesions must be identified by x-ray examination. Routine opaque enema examination is inadequate in the majority of cases. Air contrast examination, by inflation of the colon with air or oxygen after partial evacuation of the barium mixture, is the only satisfactory diagnostic procedure. Even with the most skillful technique of examination these tumors are often difficult to visualize. A second and a third examination may be necessary. Occasionally diagnosis can be established only by exploratory laparotomy and careful palpation of the colon. This becomes a justifiable procedure when repeated examination fails to demonstrate the origin of obvious continued bleeding from the colon.

The treatment of polyps of the colon is surgical removal. Lesions within reach through a sigmoidoscope may be removed through this instrument by diathermy snare if they are pedunculated, or by electrofulguration when sessile in character. The danger of perforation of the bowel wall must be recognized and avoided. All single polyps higher in the colon should be removed by laparotomy and colotomy. Treatment of multiple polyposis of the colon should consist of preliminary eradication of all polyps of the rectum, followed by ileoproctostomy and colectomy. When malignant degeneration has already occurred in the rectum, complete colectomy with permanent ileostomy is the recommended procedure. This is also the proper treatment for polyposis secondary to chronic ulcerative colitis.

When a polyp of the colon is removed by colotomy, immediate frozen-section microscopic examination is advisable, since polyps whose gross characteristics are those of a benign lesion may prove to be malignant, at times with regional glandular metastasis already present. When definite malignant degeneration has already occurred, radical resection comparable to that which would be done for more advanced carcinoma should be performed. The absence of evidence of carcinoma in the pedicle of a malignant polyp does not preclude the existence of regional glandular metastasis.

SUMMARY

1. Many if not all carcinomas of the colon and rectum originate in benign adenomatous polyps.
2. Discovery and removal of benign polyps will prevent the development of carcinoma in many instances.
3. *The cause of rectal bleeding should never be assumed to be hemorrhoids.* Proper examination to determine the source of bleeding includes anoscopic, sigmoidoscopic and barium enema examination, with air contrast study in all cases in which the cause of bleeding has not been otherwise established.

"Cancer of the Rectum," by W. H. Daniels, M.D., Chapter XXI of the California Cancer Commission Studies, will appear in this section of the August issue of California Medicine.

California MEDICINE

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Editor, DWIGHT L. WILBUR, M.D. *Assistant to the Editor*, ROBERT F. EDWARDS

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For Information on Preparation of Manuscript, See Advertising Page 2

EDITORIALS

The C.M.A. Expands

Announcement by the Council of the California Medical Association at the 1948 Annual Session that the opening of a Southern California office had been approved was cause for satisfaction to many Association members in the southern counties. Quite naturally, some of them had previously felt that the San Francisco headquarters were a long way off, in miles if not in spirit.

It is now possible to announce the opening of a Southern California office in the Subway Terminal Building, Los Angeles. Interestingly enough, the room number is 606. This office serves not only as a Southern California headquarters but is available for the use of Association employees and officers, as well as the Cancer Commission and other committees of the Association.

Coincident with the Council's decision to open this office comes the announcement that Mr. Ed Clancy has been employed as Field Secretary. Mr. Clancy is a former newspaper publisher in Ventura County and is well versed and experienced in the fields of public relations and legislation. For the past three years he has served the Association through employment by public relations counsel and has proved his value to the Association in numerous counties where he managed the "Voluntary Health Insurance Weeks" which were a major part of the overall public relations program. More recently he has gone into several counties, on request, to aid in establishing proper public relations for county societies which were faced with unusual problems.

The opening of a Southern California office and the employment of a field secretary are indicative of the expanding activities of the Association. The permanent headquarters staff now numbers nine, with a part-time director of postgraduate activities and a medical director of the Cancer Commission in addition. The addition of a field secretary brings the Association's total staff to twelve members and places the organization in a better position to serve its component county societies and their members. The growing problems of organized medicine, particularly in fields apart from scientific medicine, demand that an adequate staff organization be maintained, and it is obvious that the present personnel, both in numbers and in varieties of skills, is in a better position to do the job that needs doing.

The county societies and their members are cordially invited to avail themselves of the Association's services.

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NOTICES AND REPORTS

Imperial County Postgraduate Seminar

The C.M.A. Postgraduate Committee reports on the Imperial County Seminar held at El Centro, May 20 and 21:

MAY 20

8:00 p.m.—Cancer of the Cervix and the Fundus Uteri—William E. Costolow, M.D., Los Angeles.
General Aspects of Cancer—Lyell C. Kinney, M.D., Chairman, C.M.A., Cancer Commission.

MAY 21

10:00 a.m.—Clinical Conference: (1) Rheumatic Fever; (2) Toxemia of Pregnancy.

AFTERNOON PROGRAM

Common Pediatric Problems Encountered in General Practice—Sam J. McClendon, M.D., San Diego.
Modern Management of Common Obstetrical Problems—Ralph Hoffman, M.D., San Diego.
Pitfalls in Gynecological Surgery—Charles Isham, M.D., San Diego.
Panel Presentation—Office Gynecology, Pediatrics and Obstetrics.
Discussion Period.
Motion Picture: Normal Breech Delivery.

Sixteen members of the Imperial Medical Association attended the seminars. This is approximately 60 per cent of the membership.

The program provided an excellent summary of the recognized and accepted advances in the presented subjects and it was agreed that the committee and the physicians attending the seminars were particularly fortunate in obtaining a fine faculty. Dr. Costolow emphasized the importance of early diagnosis of cancer of the cervix and endometrium. The responsibility for this, he said, rests not only with the patient but also with the family physician whose attention to unusual symptoms, with immediate and definite diagnosis by proper physical examination and biopsy, will result in treatment of a larger percentage of cases in early stages where an 85 per cent cure rate can be expected. Dr. Kinney's discussion dealt with the increasing incidence of cancer coincidental with the extension of the life span of larger proportions of the population into the years of higher incidence of cancer. Fifty per cent of all cancer may be diagnosed by the family physician, Dr. Kinney said, and the other 50 per cent must be promptly diagnosed with the help of consultation and special examinations.

Dr. McClendon pointed out that in California there are only 335 pediatricians to serve an expanding population of approximately 10,000,000 people. The majority of pediatric care, about 75 per cent, particularly in non-metropolitan areas must therefore be supplied by physicians in general practice, he said. He discussed pediatric problems most likely to confront general practitioners. Dr. Hoffman's paper on obstetrics presented many very vital advances in this field particularly in prenatal care, in anesthesia, and in solution of operative problems. Dr. Isham outlined the most important and frequently occurring gynecological diseases and discussed the present treatment of them through uses of chemotherapy, antibiotics and surgery.

Physicians who attended the seminars requested that others be offered in the area in the fall months.

Executive Committee Minutes

Tentative Drafts: Minutes of the 208th and 209th Meeting of the California Medical Association Executive Committee.

The 208th meeting was called to order by Dr. Sidney J. Shipman, acting chairman, at 10 a.m., in Room 220, St. Francis Hotel, San Francisco, Wednesday, April 14, 1948.

1. *Roll Call:*

Present were Doctors E. V. Askey, R. Stanley Kneeshaw, Lewis A. Alesen, Sidney J. Shipman, L. Henry Garland (ex officio), members of the Executive Committee, Dr. Dwight H. Murray, chairman of the Committee on Public Policy and Legislation, Mr. Ben H. Read, executive secretary of the Public Health League of California, Mr. Howard Hassard, legal counsel, Mr. John Hunton, executive secretary, and Mr. Ed Clancy of public relations counsel.

2. *Hospital District in Porterville:*

Mr. Read discussed the situation in Porterville, where a hospital district is in process of formation and pressure is being put upon local officials to open

up the staff of the proposed hospital to various substandard practitioners. The local physicians have asked for assistance from the Association in public relations matters and on motion regularly made and seconded, it was voted to send Mr. Clancy to Porterville to survey the situation and report back to the Council with suggestions for assistance to the local members.

After further discussion of the potential dangers to high professional standards through formation of hospital districts and the use of federal or state funds as aids in hospital construction, the following resolution was made, seconded and unanimously adopted:

WHEREAS, Many California communities are in need of additional hospital facilities; and

WHEREAS, Federal and state funds are available in some cases to aid in the construction of such facilities; and

WHEREAS, Funds may also be obtained by private subscription, as has been done in many communities under properly organized campaigns; and

WHEREAS, Federal or state funds may be obtained only by following a prescribed procedure which may entail considerable delay and may place upon the hospital directorate many burdens of construction details, possibly including costly fixtures not considered essential by those who will use, own and operate the hospital; and

WHEREAS, The provision of state funds will place the receiving hospital in a position where demands may be made upon the hospital management to admit substandard practitioners to the hospital professional staff because public money has been used in aid of construction and any practitioner may claim with some cause that his patients are a part of the public; now, therefore, be it

Resolved, That the Executive Committee of the California Medical Association, the Council concurring, places itself on record as urging that funds for hospital construction be raised by private subscription and cautioning all physicians and communities to investigate carefully the disadvantages attached to the use of public funds for hospital construction, it being understood that in some instances the use of public funds may represent a necessity which permits no alternative; and be it further

Resolved, That copies of this resolution be forwarded to all component county medical societies so that these societies and their members may look into the possible disadvantages of using public funds for hospital construction and not be misled by the theory of "something for nothing."

Adjournment.

SIDNEY J. SHIPMAN, M.D., *Chairman*
L. HENRY GARLAND, M.D., *Secretary*

209th Meeting

The 209th meeting was called to order by acting Chairman Sidney J. Shipman in the Association's office at 11 a.m., Sunday, May 9, 1948.

1. *Roll Call:*

Present were Doctors Shipman, Askey, Bruck and Kneeshaw, members of the Executive Committee, Secretary Garland and Editor Wilbur, ex officio members, and Messrs. Hunton (executive secretary), Hassard (legal counsel), and Clem Whitaker, public relations counsel. Absent: Dr. L. A. Alesen (illness).

2. *Organization of Committee:*

Attention was called to the fact that the Executive Committee had not yet organized. Upon nomination duly made and seconded, Dr. Sidney J. Shipman was unanimously elected Chairman.

3. *Hospital Construction:*

Considerable discussion was held concerning the construction of hospitals with private, state and federal funds or available combinations of such funds. It was pointed out that the receipt of federal funds is through the State Department of Public Health, which designates a priority list for hospitals to receive the limited (about $1,900,000 annually) federal hospital money available to the State of California. It was also pointed out that various construction specifications are imposed before federal funds may be received and that such specifications may result in an increased construction cost. Attention was also paid to the present lack of state laws which require the maintenance of professional standards in hospitals constructed under the Hospital District Law, this lack leaving such hospitals at the discretion of the local administrative board insofar as professional staff and operating standards are concerned.

It was regularly moved, seconded and unanimously voted that the Association adopt a program to (1) amend present state laws in order to insure high professional standards in hospitals constructed under the Hospital District Law, (2) carry on an educational program with county medical societies and their members relative to the advisability of raising hospital funds by private subscription and the possibilities of impaired professional standards where public moneys are obtained for hospital construction, and (3) work toward the elimination of substandard health insurance policies now reported being sold in quantity in California.

4. *Osteopathy:*

It was reported to the committee that the California Osteopathic Associatnon has an active committee engaged in studying the possibility of a merger of medicine and osteopathy in California, that a new osteopathic school has sprung up in the state and is issuing M.D. degrees and that at least some of the osteopathic leaders in California are interested in a possible professional merger. On motion duly made and seconded, it was voted that Doctors Askey and L. A. Alesen be authorized to meet with members of the committee of the California Osteopathic Association for informal discussions of this matter.

5. *Los Angeles Office for C.M.A.:*

Mr. Hunton reported on his investigations into available office space in Los Angeles and stated that

the major medical buildings there were not able to offer suitable space at this time. He also reported that Mr. Ed Clancy of Mr. Whitaker's office now has an office in Room 606 of the Subway Terminal Building in downtown Los Angeles, with telephone answering and stenographic service available through a public stenographer from whom the office space is rented. Mr. Clancy's services have recently been in demand for legislative purposes for the Association and the Committee on Public Policy and Legislation has outlined additional work for him that will extend for a year or more. Mr. Hunton suggested, and Mr. Whitaker agreed, that under the circumstances it would be advisable for the Association to place Mr. Clancy directly on its payroll and divide his duties between legislative work and field secretarial work out of the Los Angeles office.

On motion duly made and seconded, it was unanimously voted that Mr. Clancy be employed by the Association, with headquarters in Los Angeles, and that the office he now occupies be assumed by the Association as its Los Angeles office for the use of Association employees, including the Cancer Commission.

6. *Definition of Public Health:*

The Chairman and members of the committee discussed the proposal that a definition of the scope of recognized public health activities and a delineation between public health and the private practice of medicine be arrived at. After discussion it was regularly moved, seconded and voted unanimously that such a definition be undertaken in cooperation with Dr. Wilton L. Halverson, State Director of Public Health.

7. *Proposed A.M.A. Resolution Re Rebates:*

A letter was read from Dr. Wilbur Bailey, in which he proposed that a resolution be introduced into the A.M.A. House of Delegates by the delegates from California in an attempt to clarify possible misunderstandings regarding rebating practices. It was brought out that the A.M.A. now has a committee studying rebating questions and that Dr. E. Vincent Askey is a member of that committee. It was regularly moved, seconded and voted that legal counsel prepare a letter to this committee, requesting that the committee introduce a resolution into the A.M.A. House of Delegates to establish as a part of the Principles of Medical Ethics a definition of rebating which could be applied in any state or county medical society.

Adjournment.

SIDNEY J. SHIPMAN, M.D., *Chairman*
L. HENRY GARLAND, M.D., *Secretary*

In Memoriam

ALLEN, CARLTON STEWART. Died in Los Angeles, May 4, 1948, age 64, of a heart attack. Graduate of the University of Southern California School of Medicine, Los Angeles, 1909. Licensed in California in 1909. Doctor Allen was a retired member of the Los Angeles County Medical Association and the California Medical Association.

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KIRKPATRICK, JOSEPH HUNTER. Died in Los Angeles, March, 1948, age 77. Graduate of the Chicago Homeopathic Medical College, Illinois, 1897. Licensed in California in 1897. Doctor Kirkpatrick was a retired member of the Los Angeles County Medical Association and the California Medical Association.

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LINDSAY, WILLIAM KINKADE. Died in Sacramento, May 5, 1948, age 71. Graduate of the University of California Medical School, Berkeley-San Francisco, 1901. Licensed in California in 1901. Doctor Lindsay was a retired member of the Sacramento Society for Medical Improvement and the California Medical Association.

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MACK, CLIFFORD WILMOT. Died in Livermore, March 31, 1948, age 64. Graduate of the University of Michigan Medical School, Ann Arbor, 1908. Licensed in California in 1908. Doctor Mack was a member of the Alameda County Medical Association, the California Medical Association, and an Affiliate Fellow of the American Medical Association.

PHILIP, WILLIAM STEWART. Died in Pasadena, November 29, 1947, age 82. Graduate of McGill University Faculty of Medicine, Montreal, 1889. Licensed in California in 1896. Doctor Philp was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

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ROGERS, FRANCIS LLEWELLYN. Died in San Pedro, April 30, 1948, age 83, following an extended illness. Graduate of the State University of Iowa College of Medicine, Iowa City, 1891. Licensed in California in 1906. Doctor Rogers was a retired member of the Los Angeles County Medical Association and the California Medical Association.

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SLEMONS, JOSIAH MORRIS. Died in Los Angeles, April 30, 1948, age 72. Graduate of Johns Hopkins University School of Medicine, Baltimore, Maryland, 1901. Licensed in California in 1913. Doctor Slemons was a retired member of the Los Angeles County Medical Association and the California Medical Association.

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SMILEY, HARRY WILBUR. Died in La Jolla, April, 1948, age 62. Graduate of the University of Arkansas School of Medicine, Little Rock, 1918. Licensed in California in 1920. Doctor Smiley was a retired member of the Riverside County Medical Society and the California Medical Association.

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WOODS, RALPH A. Died in Mexico City, May 5, 1948, age 56, of a heart attack. Graduate of the University of Illinois College of Medicine, Chicago, Illinois, 1920. Licensed in California in 1920. Dr. Woods was a retired member of the Los Angeles County Medical Association and the California Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Dr. Charles M. Carpenter, professor of infectious diseases in the School of Medicine on the Los Angeles campus of the University of California, has been elected chairman of the Medical Research Society of Southern California. The organization was recently formed to further high standards of medical research and education and to foster the public's interest in the present-day need of research. The group corresponds to a similar organization in Northern California.

Advisory council members are, Dr. Walter Macpherson, College of Medical Evangelists; Dr. B. O. Raulston, University of Southern California; Dr. Stafford L. Warren, University of California at Los Angeles, and Dr. Lewis T. Bullock.

* * *

Dr. Ralph Schroeder has been elected president of the newly formed San Gabriel Valley branch of the Los Angeles County Medical Association. The new group is reported seeking county medical society sanction of its formation and of a proposal to take into membership doctors who are now members of the Pasadena-Alhambra and the East Los Angeles branches of the county organization. Dr. Samuel N. Smith is vice-president of the San Gabriel Valley group, and Dr. E. E. Wadsworth is secretary.

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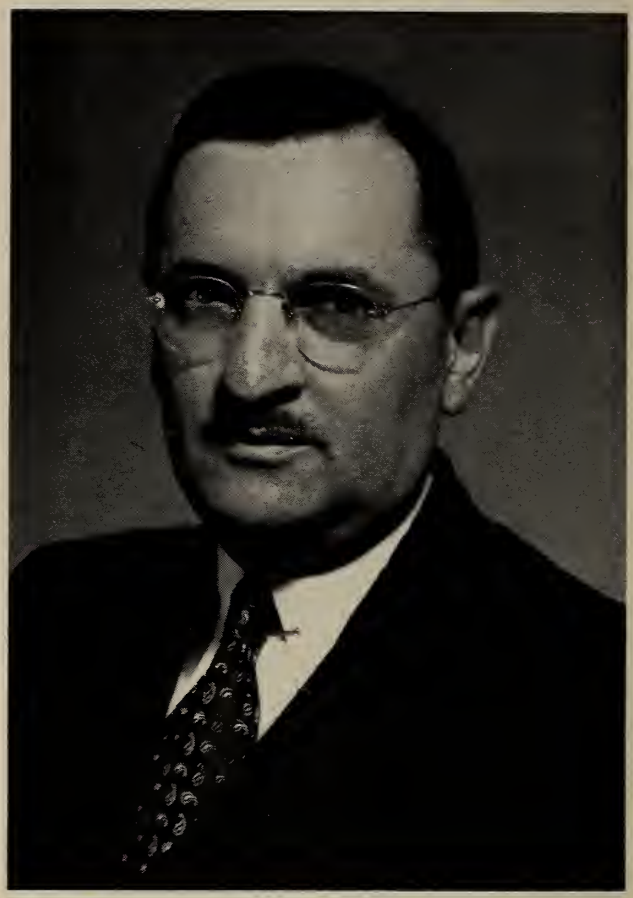
Creation of the departments of Biophysics, Infectious Diseases, and Physical Chemistry in the new University of California at Los Angeles Medical School, and the appointments of 16 physicians to the faculty have been approved by the University of California Board of Regents. The appointees are Dr. Ernest H. J. Bors, Dr. Francis X. Byron, Dr. Roger O. Egeberg, Dr. Kathryn F. Fink, Dr. Robert M. Fink, Dr. Leo Kaplan, Dr. Wright H. Langham, Dr. William H. Leake, Dr. George M. Leiby, Dr. Charles W. McClanahan, Dr. Thomas H. Sternberg, Dr. George A. Stevens, Dr. George V. Taplin, Dr. Joseph A. Weinberg, Dr. Samuel J. Weinberg and Dr. Franklin B. Wilkins. Fifteen of the 16 physicians are associates with the Sawtelle and Birmingham Veterans Administration hospitals, whose teaching and research programs are to be coordinated with similar work at the new UCLA Medical School. Dr. Langham, a member of the staff of Los Alamos Scientific Laboratories, will integrate work on atomic medicine with the medical school's program.

* * *

At the annual meeting of the Board of Trustees of the College of Medical Evangelists held May 17, 1948, Dr. George Tryon Harding, clinical professor of psychiatry at the Ohio State University College of Medicine, and Medical Director of the Harding Sanitarium in Columbus, Ohio, was elected president of the College of Medical Evangelists. Dr. Harding will take office September 1, 1948.

The Board of Trustees' report also announced that Dr. Walter E. Macpherson, for six years president of the College of Medical Evangelists and formerly its dean, will become vice-president of the College and chairman of the section on medicine.

Dr. Harding was born in Columbus, Ohio, in 1904, and graduated from the College of Medical Evangelists in 1928. At present he is a consultant in neuropsychiatry at the Children's Hospital, Grant Hospital, and University Hospital in Columbus, Ohio. He is a member of the board of trustees of the Franklin County Tuberculosis Hospital in Columbus, a past president of the Columbus Academy of Medicine, and former councilor of the Ohio State Medical Association.



DR. GEORGE T. HARDING

He was certified by the American Board of Psychiatry in 1941, and is now an examiner on that Board. Dr. Harding is affiliated with the following medical organizations: a Fellow of the American Medical Association, the American Psychiatric Association, and the American College of Physicians; a member of the Association for Research in Nervous and Mental Disease, and of Central Neuropsychiatric Association; chairman of the Mental Hygiene Committee of the Ohio State Medical Association; past president of the Columbus Academy of Medicine; and special lecturer in psychiatry in the Graduate School of Medicine of the College of Medical Evangelists.

* * *

The 34th Clinical Congress of the American College of Surgeons will be held in Los Angeles, with headquarters at the Biltmore Hotel, from October 18 to 22, 1948. The program of scientific sessions on subjects in the fields of general surgery; eye, ear, nose, and throat surgery; gynecology and obstetrics; urology; and orthopedic, thoracic, plastic, and neurological surgery, will be supplemented by operative

clinics in hospitals in Los Angeles and vicinity by showings of operations by television and motion pictures, and by a four-day hospital standardization conference for hospital personnel. Dr. Donald G. Tollefson of Los Angeles is chairman of the committee on arrangements.

SANTA CLARA

A venereal disease demonstration project, sponsored by the Palo Alto City, Santa Clara County, and San Jose City Health Departments; the County Medical Society; the State Department of Public Health; and the U. S. Public Health Service, is under way in Santa Clara County, the State Department of Public Health reports.

The purpose of the study is two-fold:

1. To demonstrate that strengthening of the private physician and health department relationship, as an essential of a sound venereal disease control program and upon a continuing basis, will result in increasing the number of patients under the care of private physicians.

2. To demonstrate that a public information program, integrated with the general health education program and upon a continuing basis, will result in accelerated case finding both for private physician and the health departments.

An executive committee is directing the project. Members of the committee are health officers Louis Olsen, Palo Alto; Dwight M. Bissell, M.D., San Jose; W. Elwyn Turner, M.D., Santa Clara County; and Joseph Donovan, Executive Secretary, Santa Clara County Medical Society. Dr. Turner is chairman of the committee.

CONTRA COSTA

Plans for formation of a countywide hospital district, which would spend $4,500,000 for acquisition, construction and improvement of facilities throughout the county, recently received the endorsement of the Contra Costa Medical Society. The endorsement was contained in a letter to the county board of supervisors. The proposed program, which would carry out recommendations made by J. E. Hamilton and Associates, hired last year to make a survey of the county's needs, includes construction of a new 150-bed general hospital in Richmond at a cost of $2,500,000 and a new 50-bed facility in the Walnut Creek-Lafayette area at a cost of $875,000, purchase of the Pittsburg Community Hospital for about $200,000 and purchase of the Martinez Community Hospital for around $450,000. All facilities included in the plan would be administered by a non-profit organization and all county residents would have access to hospitalization at cost.

SISKIYOU

Bubonic plague has been demonstrated in fleas from squirrels collected by State Department of Public Health rodent survey crews in Siskiyou County. The squirrels were collected in April.

TULARE

A petition asking that the proposed Tulare District Hospital be made available to all licensed physicians and surgeons when it is ready for use was presented to the board of directors of the hospital district last month by Harry Bussard, D.O. He said that the petition had been signed by residents of the district "who feel that since the hospital is tax supported by them they should be privileged to have osteopathic physicians and surgeons available, as well as medical physicians and surgeons."

GENERAL

The California State Personnel Board announces examinations will be held August 3 for applicants for the positions of physicians and surgeon and senior physician and surgeon. Salary range for physician and surgeon is $415 to $505 a month, and for the senior position is $530 to $644 a month. Details of the requirements and description of the positions may be had from State Personnel Board, 1015 L Street, Sacramento.

* * *

An appeal for doctors to fill vacancies anticipated in the medical branch of the Veterans Administration was made recently by H. H. Darling, M.D., acting Medical Director for the Branch 12 area, in a letter to the California Medical Association. Pointing out that the doctors who were assigned to the Veterans Administration from the Army and Navy at the end of the war soon will complete their obligated tour of military duty, Dr. Darling said that it will require a major effort to replace them. In Branch 12, he said, which encompasses California, Nevada, Arizona and Hawaii, "there is a critical need for anesthesiologists and men who are interested in tuberculosis."

Stressing the opportunities for young physicians, Dr. Darling called attention to a recent statement by Dr. Paul Magnuson, Chief Medical Director, in which he said: "I know of no place in the country, other than the Veterans Administration hospitals, where a man can practice 80 per cent of the time in a specialty after finishing a three-year residency." In relation to Dr. Magnuson's statement, Dr. Darling said that "in general, the specialty boards require that at least 80 per cent of a candidate's practice be devoted to a specialty for at least two years after completion of formal residency training."

"The compensation of doctors in the Veterans Administration is based directly on qualification," Dr. Darling said in his letter. "Original appointment is in the grade commensurate with the applicant's training and experience. There is no rigid organizational pyramid. Initial basic salaries range from a minimum of $4,149.60 per annum for men who have had less than three years' experience, including internship and civil and military practice, to a maximum of $9,975.00 per annum. There are statutory provisions for periodic increases in salary up to $11,000.00 per annum for Diplomates of the American Specialty Boards, and $10,000.00 for others. Board men, whatever their grades, receive a 25 per cent addition to the base pay, up to the statutory maximum. Some of our hospitals have quarters available with exceptionally low rental. Leave and retirement privileges are most liberal."

Doctors interested in further information concerning available opportunities in hospitals or out-patient clinics, either in Branch 12 or elsewhere in the United States, may communicate with Branch Medical Director, Veterans Administration Branch Office 12, 180 New Montgomery Street, San Francisco 5, California.

* * *

A number of changes in requirements of the American Board of Obstetrics and Gynecology, Inc., were made at the annual meeting of the organization last month, according to an announcement by the Board. Bulletins now available for distribution upon application give details of all new regulations. These relate both to candidates and to hospitals conducting residency services for training.

The next scheduled examination (Part I) written examination and review of case histories, for all candidates will be held in various cities of the United States and Canada on Friday, February 4, 1949. Application may be made until November 1, 1948.

BOOK REVIEWS

DISEASES OF THE SKIN. By Oliver S. Ormsby, M.D., Rush Professor of Dermatology Emeritus, University of Illinois, and Hamilton Montgomery, M.D., M.S., Associate Professor of Dermatology and Syphilology. Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester. Seventh Edition. Lea & Febiger. 1948.

Ormsby's textbook, always the old reliable in dermatology, has been brought right up to date in this 1948 seventh edition. The authors have done a most thorough job of incorporating in it the recent advances in dermatology; almost every page indicates a thorough study of the newer and correct literature.

The junior author, particularly well known for his work in histopathology, has rendered an invaluable service by thoroughly covering the field of laboratory diagnosis.

The bibliography, carried at the bottom of the pages, is quite voluminous and hence of value for careful study of a given subject.

Every physician or student who is interested in dermatology-syphilology should have this new edition in his library.

PSYCHOBIOLOGY AND PSYCHIATRY—A Textbook of Normal and Abnormal Human Behavior. By Wendell Muncie, M.D., Practicing Psychiatrist; Chairman, Medical Advisory Board, Seton Institute, Baltimore, Md. Second Edition with 70 illustrations. The C. V. Mosby Company. 1948.

By far the most striking change in this edition from the first is the color of the cover from blue to red. In addition, by employing thinner paper and eliminating the lengthy historical survey at the end, the bulk of the volume has been materially reduced. The convulsive disorders have graduated to the dignity of chapter treatment, and an additional short chapter treats of newer physical treatment methods, namely shock and leucotomy. In other respects there is little difference in the two editions.

One might have hoped that one so closely associated with Adolf Meyer would present a clear and understandable exposition of this school of Psychiatry. In this reviewer's opinion this has unfortunately not been accomplished. One finishes this book with the firm opinion, in spite of the author's protestations to the contrary, that the main virtue of Psychobiology is its eclecticism, its greatest vice the introduction of still another terminology to confuse the student.

The presentation of case material to illustrate the various reaction types is excellent, and the special terminology of the Psychobiologist is sufficiently explained and paralleled with more familiar terms to clarify the classification in this regard.

Those conditions which it is now fashionable to consider as "psychosomatic" are given adequate treatment. The author remains non-commital in failing to give a definite opinion regarding the primary importance of specific constitutional and environmental factors in the production of these entities, which at the present time seems the wise and conservative thing to do.

THE TREATMENT OF RHEUMATISM IN GENERAL PRACTICE. By W. S. C. Copeman, M.D. Fourth Edition. The Williams & Wilkins Co. 1946.

This is the fourth edition of a book first published in 1933, and, as the author writes in his preface, makes no pretense of being a textbook. Even so, a wide range of subjects is included, some of which, e.g., the chapter on endocrines, could be deleted. Part I is a discussion of rheumatic fever, which omits mention of the relationship of streptococcal infection to this disease. The chapter on rheumatoid arthritis, only 17 pages, contains a wealth of information.

There are contradictory passages in different sections on diet and many drugs recommended which are no longer used by well-informed physicians in the United States. The book has little to recommend it to the general practitioner; the specialist on rheumatic disease will find in it some interesting material.

EPILEPSY, The Annual Symposium of the Association for Research in Nervous and Mental Disease. Proceedings of the Association held jointly with the International League against Epilepsy, December 13 and 14, 1946, New York. Research Publications Association for Research in Nervous and Mental Disease. Volume XXVI. Editorial Board, William G. Lennox, M.D., H. Houston Merritt, M.D., and Thomas E. Bamford, M.D. With 167 Illustrations and 56 Tables. The Williams & Wilkins Company. 1947.

This book of 650 odd pages, 167 illustrations and 56 tables presents the latest studies and opinions on Epilepsy by the outstanding authorities on this subject in this country and abroad. The volume consists of 45 papers dealing with almost every phase of convulsive disorders, including sections on the historical aspects of the subject, heredity and pathology, experimental studies, electroencephalography, treatment, special contributions from the experience of the recent war and, finally, the psychological and social aspects of Epilepsy. Especially valuable are the questions, answers, comments and discussions appended to a high percentage of the contributions. The quality of this forum of discussion can be appreciated from the fact that the names of such authorities as Lennox, Penfield, Merritt, Walker, Gibbs, Fulton, Cobb, McCulloch and Jasper appear again and again.

As the third symposium on Epilepsy in the 26 annual meetings of the Association for Research in Nervous and Mental Disease since 1920, the volume amply reflects the wide interest and rapid advances made in this subject since the previous symposiums of 1922 and 1929. Particularly noteworthy are the contributions in three aspects of the subject; the physiological and biochemical basis of convulsive disorders as determined by experimental methods (17 contributions), the advances in both experimental and clinical studies made possible by electroencephalography (24 contributions) and the great advances in anti-convulsive therapy, which have been achieved by neurophysiological and experimental pharmacological methods (7 contributions).

From the standpoint of fundamental pathogenesis, the electrolyte studies of Colfer, the biochemical studies of Gurdjian, Webster and Stone and the biochemical and enzymatic studies of Pope, Morris, Jasper, Elliott and Penfield were of special interest. In another paper Penfield and Jasper propose and adduce evidence to support the interesting theory that the diencephalon is "the highest level" of cerebral function to which the cerebral cortices serve a subservient role. They propose that as a central system, the diencephalon acts to unify and integrate the activity of the more specialized cortical areas in the two hemispheres.

Experimental reproduction of the electroencephalographic pattern typical of petit mal was achieved by Jasper and Droogleever-Fortuyn by stimulation of the massa intermedia and by Chenoweth and St. John following the intravenous administration of fluoroacetic acid. Additional papers of electroencephalographic importance were the frequency analyzer of Grey Walter and the increased incidence of seizure discharges and epileptic foci in epileptic patients when the electroencephalographic recording was obtained by Gibbs and Gibbs with the patient asleep. The papers on Mesantoin by Kozol and by Loscalzo and on the tridione by Davis and Lennox were of particular interest to the pharmacologist and the neurologist.

Because of its character this volume would be of but limited interest to the medical student who might better approach the subject of Epilepsy in a more orderly fashion as presented in any of the several excellent neurological textbooks now available, as for example in "Diseases of the Nervous System" by Russell Brain. For the more advanced student and the physician concerned with the convulsive reactivity of his patients, the volume should prove both stimulating and rewarding. For the neurophysiologist, electroencephalographer, neurologist and neurological surgeon, the book definitely is a "must."

OFFICE IMMUNOLOGY, Including Allergy. A Guide for the Practitioner. Edited by Marion B. Sulzberger and Rudolf L. Baer. Authors: Marion B. Sulzberger, M.D., Professor of Clinical Dermatology and Director, New York Skin and Cancer Unit, New York Postgraduate Medical School and Hospital; W. C. Spain, M.D., Clinical Professor of Medicine, New York Postgraduate Medical School and Hospital; Rudolf L. Baer, M.D., Instructor in Dermatology and Syphilology, New York Skin and Cancer Unit, New York Postgraduate School and Hospital; Abram Kanof, M.D., Adjunct Pediatrician, Jewish Hospital, Brooklyn; Alfred J. Weil, M.D., Lederle Laboratories Division, American Cyanamid Company; Naomi M. Kanof, M.D., Associate Attending in Dermatology, Garfield Memorial and Children's Hospitals, Washington, D. C. The Year Book Publishers, Inc., Chicago. 1947. Price, $6.50.

Office Immunology is a clinical handbook containing the essential information regarding immunologic procedures indispensable in the diagnosis and treatment of allergic and infectious diseases. The authors, combining the experience of the dermatologist, allergist, pediatrician and immunologist have selected with careful discrimination the material which should be included under this title. Controversial ideas and methods have been excluded. The immunologic procedures described, include only those which can be performed on the patient by the practicing physician without complicated laboratory facilities. The technics of performing the tests and the criteria for evaluation of results are described in detail.

The range of subject matter is indicated by the chapter headings. The book begins with two chapters devoted to descriptions of the common technics of diagnosis, prophylaxis and therapy. Then follows chapters on the immunology of infections; the immunologic principle of transfusion reactions and the Rh factor; the respiratory allergies; dermatologic immunology; immunologic management of spider, insect and snake bites; and finally a chapter on miscellaneous allergies. The chapter on infectious diseases contains not only the important facts on the diseases described, but also, a useful compilation of detailed specifications of immunologic preparations, including the name of the supplying firm, complete information regarding packaging, dosage schedules, etc.

Study of this book re-emphasizes the numerous and indispensable uses of immunologic methods in the day by day practice of medicine. Office Immunology is unique in the wide range of useful information included in one volume. It should be a useful addition to the desk library of the general practitioner. internist, dermatologist, pediatrician and even the allergist.

HEADACHE AND OTHER PAIN. By Harold G. Wolff, M.D., Professor of Medicine (Neurology) and Associate Professor of Psychiatry, Cornell University Medical College. Oxford University Press. 1948. $12.00.

Considering the relative frequency of headache as a presenting symptom, the practitioner of medicine should be delighted by the advent of a treatise of over 600 pages devoted solely to this subject. Most of us are familiar with one or another aspect of the researches of the author and his coworkers on the general subject of pain. They have accomplished much in controlling experimental procedures in a phenomenon which must, by definition, remain in the last analysis subjective.

The first part of the book deals with the mechanism of pain in general. Following this is an exhaustive treatment, from the experimental aspect, of pain-sensitive structures in the head, based on careful observations made during neurosurgical procedures. The remainder deals in detail with the type and mechanism of head pain in those conditions, varying from cerebral neoplasm to dental caries, in which headache is a striking symptom.

Migraine receives extensive treatment, both from the standpoint of the physiological mechanism of the production of its symptomatology and the personality structure in which it is prone to develop. For the consideration of this syndrome alone the book is well worth reading.

The author's approach to the subject is far from being confined to the theoretical; treatment of the patient is given adequate consideration. In all, the book can be highly recommended to the profession at large. For the neurologist and psychiatrist it is extremely valuable.

HISTORY OF THE MEDICAL SOCIETY OF THE COUNTY OF WESTCHESTER, 1797-1947. Published by the Medical Society of the County of Westchester, 1947. Cloth bound, 193 pages.

The history of this county medical society of over 1,000 members was published in honor of its one hundred and fiftieth anniversary, dedicated to its two past historians, and compiled by its present historian. Dr. Lawrence D. Redway.

The first county medical society in the state of New York began: "at a respectable Meeting of Physicians of the County of Westchester on the 8th day of May, 1797—at the House of William Barker in the White Plains—Present—" The names of the eight founding fathers followed.

The book is divided into two parts. Part I consists of an interesting historical sketch of the period prior to the society's inception and through it until 1922. Part II. the larger portion of the book, is devoted to a year-by-year factual report of the society's activities from 1922 to 1947, and includes the records of the articles of incorporation of the society and the reason therefor, at the surprisingly late date of 1935. Since the minutes of the society from 1779 to 1831 were unaccountably "lost," the records of its medical men and events for that period were gleaned from the newspapers of the county and from other sources.

The book is well annotated and documented and will be of inestimable value for future historical reference.

THE ACUTE BACTERIAL DISEASES—Their Diagnosis and Treatment. By Harry F. Dowling, M.D., F. A. C. P., Clinical Professor of Medicine, George Washington University; with the collaboration of Lewis K. Sweet, M.D., Chief Medical Officer in Pediatrics and Infectious Disease, Gallinger Municipal Hospital. W. B. Saunders Company. 1948. $6.50.

Descriptions of the important bacterial infections currently available in medical textbooks are confusing and incomplete. None has segregated these important disorders on the basis of the etiological agents. This new book by Dowling is a most important contribution. A preliminary section is devoted to the principles of diagnosis and treatment of the acute bacterial infections. This is followed by a detailed consideration of the diseases caused by the various infectious agents.

Only minor criticisms of any part of the work are indicated. The treatment of subacute bacterial endocarditis is not described in sufficient detail in the light of present information. The type of renal lesion associated with sulfonamide therapy which is not caused by precipitation of crystals in the renal tubules but by a diffuse process presumably the result of sensitization to the drug, is not mentioned. This is a serious oversight since this complication cannot be prevented by increasing the flow of urine or by the administra-

tion of alkali. Recent developments in the field of penicillin therapy involving less frequent administration of the ordinary soluble form of the drug were not available at the time the book went to press.

This book should be in the library of all physicians and medical students. It will be of particular value to the latter group and to their teachers, since the information presented has not been readily available elsewhere.

BERGEY'S MANUAL OF DETERMINATIVE BACTERIOLOGY. Board of Editor-Trustees Robert S. Breed, New York State Experiment Station (Cornell University), Geneva, New York; E. G. D. Murray, McGill University, Montreal, Province Quebec, Canada; and A. Parker Hitchens, University of Pennsylvania, Philadelphia, Pennsylvania. Sixth Edition. The Williams & Wilkins Company. $15.00.

The sixth edition of Bergey's Manual brings this well known and valuable guide to the classification of the bacteria up to date. The book has been expanded to include additional species and new information. An index of "Sources and Habitats" will be of particular value in the identification of unknown organisms. Inspection of several sections reveals the considerable confusion that still exists in regard to the delineation of species among the bacteria and viruses.

This volume is an essential tool for general bacteriologists. It is much less valuable for the medical bacteriologist since better and more usable descriptions of the human pathogens are available.

HANDBOOK OF TREATMENT AND MEDICAL FORMULARY. By Charles M. Bruber, Ph.D., M.D., Professor of Pharmacology, Jefferson Medical College, Philadelphia. F. A. Davis Company, Publishers, Philadelphia. 1948. $7.00.

This book is written as a reference work and a guide in drug prescription therapy. Its reasons for being in existence are the rapid advance in drug therapy and the need for ready and concise reference on the part of the medical practitioner. Its intent is to assist the practitioner to recognize anachronistic medicine and to employ modern methods.

The conditions discussed are arranged alphabetically. There is abundant cross reference. The drugs used in treatment are usually given in the form of prescriptions. The prescriptions are written out in both English and Latin. (The author rightly assumes that the full Latin rendition will be instructive to many.) Doses are given in both the metric and apothecary systems.

As a summary of modern drug therapy—up to 1945 (there are few references past that year)—one may praise this book, even if one does not agree with all of the selection of remedies. For example, why should pellet implantation be the only form of testosterone therapy used for eunuchoidism and testosterone in oil the only form used in cryptorchidism? On the other hand, it is refreshing to read all through the treatment of abrasions of the skin and subcutaneous abscesses and see no recommendation of the old type of skin disinfectant; instead one is advised to make the wound as clean as possible, to cover it and to use penicillin or sulfathiazol topically.

It is a handy book to have in one's office.

THE 1947 YEAR BOOK OF OBSTETRICS AND GYNECOLOGY. Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., Professor of Gynecology, Cook County Graduate School of Medicine. The Year Book Publishers, Chicago. $3.75.

Testing one's familiarity with the current literature, it is a great stimulus to read every summary and comment of *The 1947 Year Book of Obstetrics and Gynecology* so ably edited by Dr. J. P. Greenhill. From the first article "Fibrous Nature of Human Cervix and Its Relation to Isthmic Segment in Gravid and Nongravid Uteri" by Danforth (which, by the way, is a real contribution to the literature on this infrequently discussed subject) to the last division on "Endocrinology," one finds a crystal-clear, brief summation and comment on the world literature. The conservative attitude concerning the value of the hormone test for pregnancy, the use of Vitamin E in sterility, abortions, premature labor, the limitations of the application of estrogen therapy and the comments on his own article, make one feel that the author is sound and honest in his opinions. Even an editorial prerogative, however, should not extend to such a selective interpretation of the use of spinal anesthesia in obstetrics. As enthusiastic as one may become about local anesthesia and as adept as one may be in its application, it has not been accepted as the anesthetic of choice in most clinics outside of those of the "Chicago group."

The outstanding articles in obstetrics reviewed in this book are Danforth's chapter on "Physiology," Hertig's and Sheldon's "Hydatidiform Mole," "Pregnancy in Patient with Hypertensive Disease" by Chesley and Annitto, and also Brown's and Mengert's "Recognition of Midpelvic Contraction." In Gynecology the chapter on "Infertility" has many helpful suggestions. In the section on Operative Technique, Shaw's article on the "Anatomy of the Vagina" is extremely valuable. Under Malignant Tumors, the work on vaginal smears is completely reviewed and emphasis is definitely placed on its limitations.

The articles by Norman F. Miller and Emil Novak on Carcinoma of the Corpus and Uterus are outstanding and the comments are most valuable.

The author and the publisher are to be complimented again for this excellent survey and the obstetrician and gynecologist who did not read the current literature as it was published, can relieve his professional conscience by reading *The 1947 Year Book of Obstetrics and Gynecology.*

CLINICAL TOXICOLOGY. By Clinton H. Thienes, M.D., Ph.D., Professor of Pharmacology and Head of the Department of Pharmacology and Toxicology, School of Medicine, University of Southern California, Los Angeles, Calif., and Thomas J. Haley, Ph.D., Fellow in the Department of Pharmacology and Toxicology, School of Medicine, University of Southern California, Los Angeles. Second Edition. Enlarged and thoroughly revised, illustrated. Lea and Febiger. 1948.

This book is 64 pages longer than the senior author's first edition. The increases have been made in descriptive material and in the number of tests for identifying the new drugs such as dihydromorphinone (dilaudid), ephedrine isomers, demerol, etc. New tests for several old poisons are included. The new antihistamines, benadryl and pyribenzamine, are recommended for use in histamine poisoning; BAL (2, 3-dithiolpropanol) for metallic poisoning. The new insecticide, D.D.T., is also described and treatment indicated. There are two long lists of reactions of leading sulfonamides. Poisoning from vitamins is not overlooked, the two chief offenders being thiamine (B^1) and vitamin D.

This is more than a handy reference book on all aspects of poisons. There is a synopsis of all essential information about each drug. This is repetitious of the discussions in textbooks on pharmacology. The grouping of poisons according to their major toxic action is preserved from the first edition. The authors state that for each poison at least one of the treatments suggested should be available to the physician in time of emergency, and this seems to be adhered to throughout. Highly commendable features are sections devoted to chemical diagnosis, the tests being described with adequate discussions and details of use of apparatus and reagents, with remarks as to the limitations of and errors in devices, instruments, etc. There is also an appendix which describes the preparation of special reagents—information not readily found elsewhere.

While this book will be of interest chiefly to professional toxicologists, medico-legal experts, and clinical pathologists, there is enough in it of value to physicians in practice to justify having it on the office shelf of handy books.



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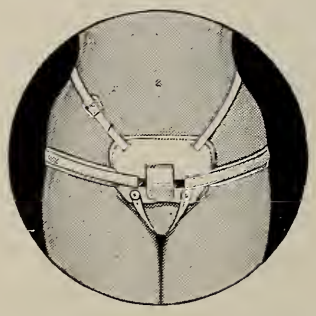
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LEAVE SOME DOCTORS FOR CIVILIANS NEXT TIME, PHYSICIAN ASKS

The greatest challenge confronting Congress and the medical profession today is "the proper and adequate provision for the care of the great number of horrible civilian casualties that are promised if World War III is to come."

This statement was made recently by Dr. James C. Sargent, Milwaukee, before the Armed Services Committee of the House of Representatives in expressing opposition to parts of Section 4 of H.R. bill No. 6274. This bill as now worded would authorize the President, pursuant to requisitions submitted by the armed forces, to draft physicians above the age of 25 stipulated as basic in the proposed law.

"To give to the Military Establishment carte blanc as this bill proposes to do, would surely lead to the same over procurement of medical personnel as before," Dr. Sargent said. "And if another war is to come—biologic and atomic warfare this time—large disaster areas with terrible civilian casualties must be expected and must be adequately provided for if the Nation is to survive.

"Ordinary civilian pursuits, agriculture and especially industry—the very foundations of our national war strength—will never survive the high casualties in store for them in another war if civilian doctors are to be thinned down again to the one to 1,500 ratio that was reached during the last war.

"The special provisions in Section 4 (c) and (d) of H.R. 6274 set the pattern for just such an unsafe distribution of physicians and set the stage for just such a national catastrophe."

Dr. Sargent is chairman of the American Medical Association's Council on National Emergency Medical Service. With but one exception, eight of the nine members of the Council, including Dr. Sargent, served in the Armed Forces during the recent war. The other member served as one of the five directors of the Procurement and Assignment Service, the agency through which 60,000 civilian physicians were recruited during World War II.

The Armed Services Committee of the House of Representatives were told that a survey made by a special committee of the A. M. A. of some 50,000 doctors revealed:

1. There were far more civilian physicians procured for the armed services during World War II than were effectively needed or used.

2. The subtraction of this large group of physicians from the civilian population left a shortage that was dangerously acute and sorely noticed despite the remarkably healthy state of the nation throughout the war years.

"A national tragedy would surely have occurred had we experienced an influenza epidemic like that following World War I or had we suffered civilian war casualties such as the bombed countries of Europe experienced in World War II," Dr. Sargent said.

The Council chairman added that "if the nation is to survive another war there can be no brooking the waste of medical talent that prevailed in the Army, Navy and Air Force throughout the war just passed." Happily, he said, the Military Establish-

(Continued on Page 38)

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LEAVE SOME DOCTORS FOR CIVILIANS NEXT TIME, PHYSICIAN ASKS

(Continued from Page 34)

ment, from the Secretary of Defense down, is working toward far better use of the medical personnel and facilities of the three services.

The studied belief of the Council on National Emergency Medical Service and the Board of Trustees of the American Medical Association, stated Dr. Sargent, is that a special provision in the law for the drafting of doctors is "both unnecessary and unwise."

"Because of the accelerated program of medical education carried on during the war years, doctors are graduating today well under the age of 26. Through this circumstance, doctors made available under the general draft provisions of H.R. 6274 would be wholly adequate to meet the numerical requirements of medical officer personnel for the increased strength of the armed forces authorized in the bill."

The point is raised, and properly so, that this would furnish only young, recently graduated physicians. That there is need for some older physicians of special talent is obvious. Such need cannot be great, however, considering the fact that this bill provides for a peace time expansion of the armed forces that does not contemplate heavy casualties of war and, important to note, provides for the medical care of young men in the prime of life and hand picked for their physical fitness.

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(Continued on Page 42)

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*Levine, S Z.: J.A.M.A. 128:283, May 26, 1945

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LEAVE SOME DOCTORS FOR CIVILIANS NEXT TIME, PHYSICIAN ASKS

(Continued from Page 38)

posed legislation, to provide the expert services of experienced physicians and surgeons needed for the expanding Army, Navy and Air Force. The Veterans Administration has pioneered in the use of highly skilled specialists in civilian practice as part-time consultants and the unprecedented excellence of the care that is being given veterans today under such a system merits the serious notice of the Military Establishment.

"Today each city of size in America holds able and thoroughly experienced specialists of every category who are not too deeply rooted to consider rejoining the military as a career were such service made somewhat more attractive. But they recall the barrier that age placed against obtaining rank and pay that was commensurate with their exceptional talents. And they recall the withering experience of long periods of inactivity and of non-medical duties."

Doctors, both in and out of service must have clinical medical work to challenge their abilities and keep them professionally alive. While there are certain real inducements to attract able medical talent to a career in military medicine they simply are not enough. Purely administrative changes, dealing with rank and duty assignment, could and would over night minimize the medical personnel problems that so concern the armed services today.

"And in the end, if neither of those means are to be employed and experience proves that soldiers and sailors are in need of medical care the profession of America will see they get it, draft or no draft. They did it handsomely in the last war, as, indeed, they always had before. And they would do it again."

SURGEONS DEVELOP NEW TECHNIQUE TO REMOVE FOREIGN BODY

Two Indianapolis doctors have developed a new technique for removing solid bodies lodged in the esophagus, the tube that leads from the throat to the stomach. The doctors are: W. D. Gatch and W. F. Molt.

Writing in the current issue of the Archives of Surgery, published by the American Medical Association, the doctors report the case of a man 46 years of age who swallowed his upper denture. They made a small opening in the stomach, passed an instrument upward into the esophagus, grasped the object and removed it through the stomach opening.

This method of removing solid bodies lodged in the lower part of the gullet, they explained, avoids the dangerous and often impossible method of extraction through the mouth with forceps. This accident is especially dangerous when the object swallowed has sharp points.

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HYGEIA EDITOR URGES CONTINUED FIGHT AGAINST DISEASES

"Medicine needs the support of understanding people who participate with their gifts and with their hours of work," states Dr. Morris Fishbein, editor of *Hygeia*, the health magazine of the American Medical Association. Writing in the current issue of the magazine, Dr. Fishbein states in full:

"Once upon a time the battle against tuberculosis, cancer, heart disease and the crippling diseases was exclusively a doctor's fight. Once upon a time the words 'cancer' and 'syphilis' were not mentioned in public gatherings because of the fear or disgust they might arouse in the minds of men and women.

"Then came the realization that a single group of the population could not win the fight alone. Now we have evolved in the United States a system of attack peculiar to the American way of life. Medicine and the public and leaders in public health and educators and philanthropists join together in a common cause against the foes that threaten the lives of human beings.

"Fifty years ago Osler called tuberculosis the captain of the men of death. Weapons in our battle against tuberculosis were the discovery of the causative organisms of tuberculosis; the discovery of the way by which tuberculosis is spread; the discovery of public health methods which would isolate the patient who spreads tuberculosis and keep him from contact with those easily susceptible to the disease; the development of a new chemotherapeutic technic for attacking tuberculosis in the human body; the

(Continued on Page 54)

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**Krasno, L., Karp, M., and Rhoads, P. S., (1948), Inhalation of Dust Penicillin, Ann. Int. Med., 28: 607-617, March.*



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HYGEIA EDITOR URGES CONTINUED FIGHT AGAINST DISEASES

(Continued from Page 46)

experimentation with BCG as a means of inoculating people against the disease.

"Today tuberculosis is seventh in the list of causes of death in the United States. The scientific progress has been carried over to the people through the medical profession, public health agencies, sanatoriums and hospitals. The funds have come from the people, from governmental agencies, from the sale of Christmas seals and the efforts of the National Tuberculosis Association.

"In the United States we have made tremendous advances against infant mortality by studying the diseases of infancy, by control of milk and water and the food supply, by proper study of nursing care of babies, by the care of premature infants.

"Our infant mortality rate has moved far down in the list of causes of death. There has been and there is being more and more suitably coordinated and well integrated action by the professions concerned, governmental agencies and voluntary associations.

"The medical profession and public health officials recognize today the need for public support in the great battles that lie ahead against heart disease, cancer, accidents, degenerative diseases of blood vessels and kidneys, crippling diseases and conditions involving the nervous system.

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SURGERY HELPFUL IN EARLY LUNG CANCER

Patients suffering with cancer of the lung have a good chance of recovering if the malady is diagnosed early enough to be treated by surgery, Edward D. Churchill, M.D., of Boston, reports in a recent issue of *The Journal of the American Medical Association.*

"The constructive results of surgical extirpation are favorable when compared with other visceral malignant tumors, and, more important, steady improvement is being recorded," according to Dr. Churchill, who adds that one or two out of every five lung cancer can be treated surgically.

Discussing the operative mortality rate of the disease, he says that this has been steadily reduced as technical problems were solved and more favorable stages of the disease recognized.

Much progress is also being made in the diagnosis of lung cancer, the Boston physician reports, adding that "there are many reasons to believe that the time lag between onset and recognition will be still further reduced."

Cancer of the lung is almost as common as cancer of the stomach. Its greatest incidence is in men (80 to 85 per cent of all cases) between the ages of 40 and 70.

Dr. Churchill says nothing is known about the cause of the disease that can be translated into effective preventive measures.

In contrast to the suggestion by some investigators that there is a relationship between cigarette smoking and lung cancer, he says that "a careful recording of the smoking habits of patients with the disease provides no factual evidence on which advice to give up smoking can be based."

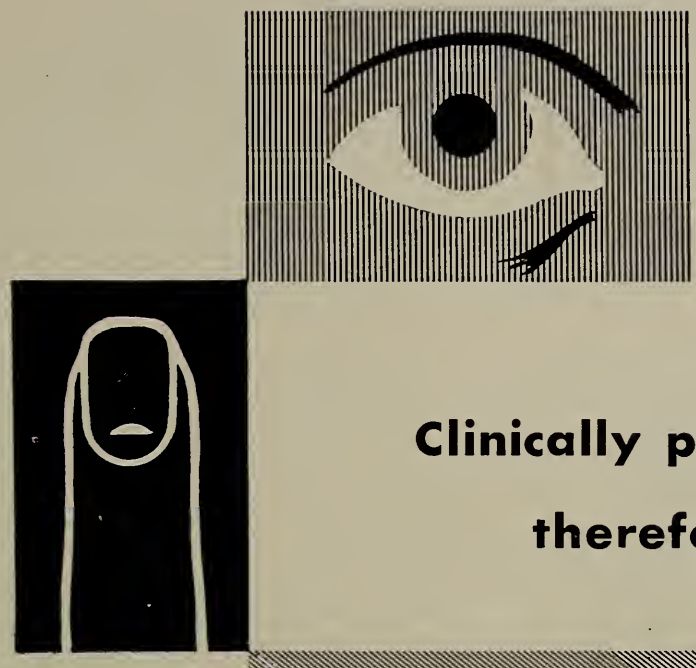
Since so little is known about the cause of cancer, physicians must at present depend upon early detection, rather than prevention, as a means of elimination of the disease. According to Dr. Churchill, the responsibility for early diagnosis of lung cancer rests not only with the general practitioner, but with all physicians regardless of their specialty.

In this connection, he cautions that the early signs of lung cancer may be so commonplace that they may not be taken seriously by either the patient or his physician.

Among the commoner symptoms of the disease is a cough which "hangs on" in an unaccustomed manner. This is the first symptom in over half of all lung cancer cases, and is a common manifestation sooner or later in 90 per cent of all cases.

Other symptoms include blood in the sputum, occurring in 40 to 50 per cent of all cases, loss of weight, pain in the chest, wheezing and swelling of the fingers and toes.

X-ray screening is considered the only practical way for the physician to detect lung cancer in the apparently well population, since this method discloses growths which may be present on the outside parts of the lung. According to the report, the increased use of x-ray screening for tuberculosis as a public health measure is bringing a few of these asymptomatic cases to light.



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WRITER URGES NEW PHILOSOPHY ON HAIR

The man with the receding hairline and balding pate can console himself with the thought that the hair he has lost wasn't good for much to begin with, according to an article in the current issue of *Hygeia*, the health magazine of the American Medical Association.

Miss J. V. Sheppard, Oak Ridge, Tenn., author of the article, says that hair has little practical use. It is not much more than a limp, vegetative growth, made up of a pouchlike root imbedded in the skin and a long shaft which is composed of horny, skin-like cells, and, so far as is known, it does not receive nourishment from the body.

Those who bemoan their paucity of hair as indicative of a lack of manliness may also take solace from Miss Sheppard, who says that the notion that a lot of hair in men expresses physical strength or virility is ancient superstition.

Primitive people believe that their hair contains a sacred spirit, and among many tribes there is a taboo against hair-cutting. Caesar made the Gauls trim their locks as a token of submission and the American Indians scalped their victims to deprive them of evil spirits supposedly inhabiting the hair.

For those who are still unconsoled by all of this and feel that baldness adds nothing to their appearance, Miss Sheppard sounds a discouraging note.

The cure of baldness, she says, depends largely on the cause. If it is the senile type, which results from the deterioration of all body cells, there is no hope of restoring the hair.

(Continued on Page 16)

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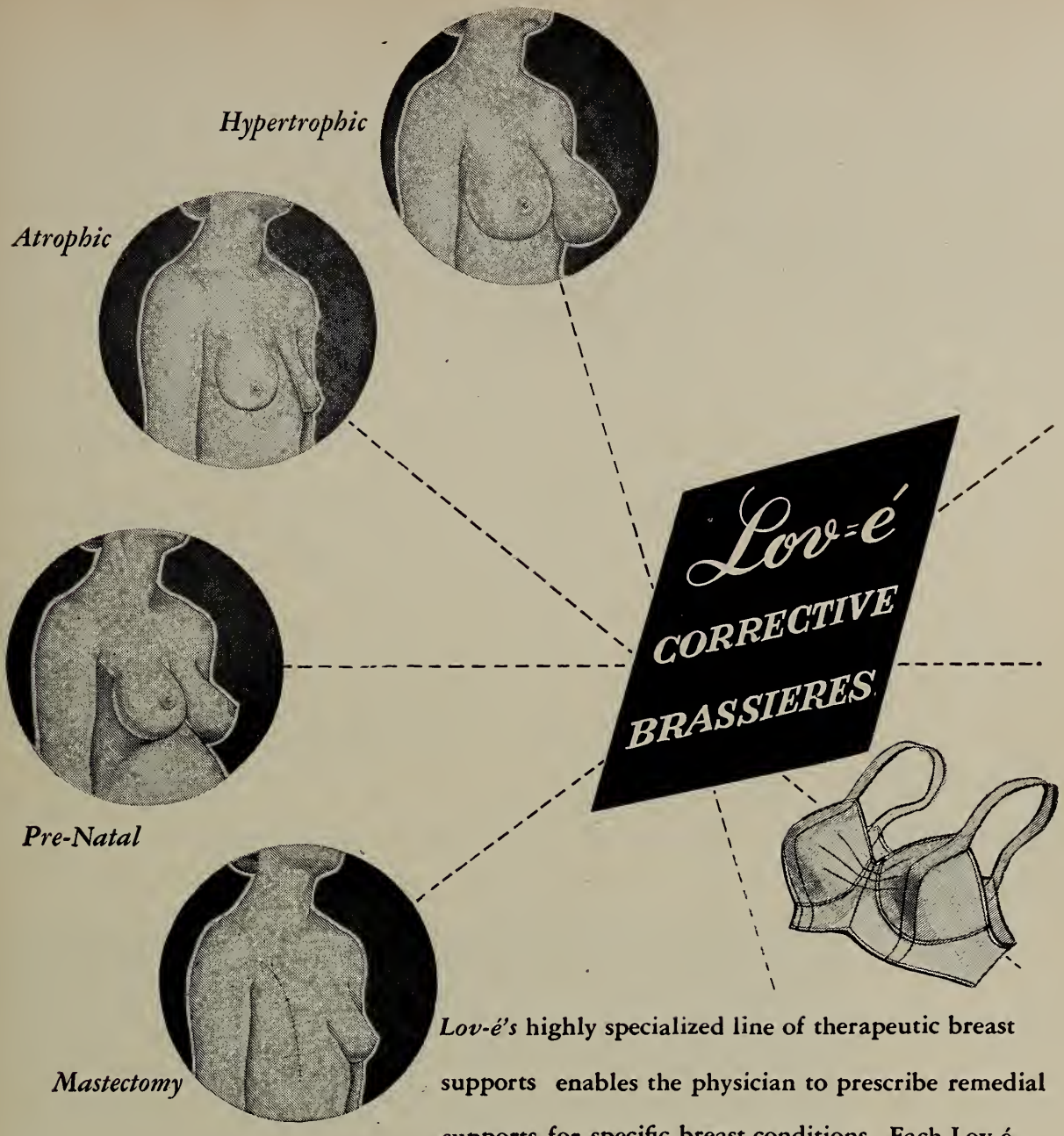
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WRITER URGES NEW PHILOSOPHY ON HAIR

(Continued from Page 12)

The outlook is also dark for premature baldness, most of which is inherited and for which, according to the article, "there is no hope" of cure.

For baldness due to the presence of microbes in the scalp, little can be done to restore the lost hair, but early treatment under the advice of a physician can do much to prevent further loss. The microbes which cause baldness thrive in oily scalps, and, in this connection, the writer recommends daily care of the hair and scalp, including adequate brushing and shampooing, as a good preventive measure.

Hormone therapy is no panacea for hair restoration, either, Miss Sheppard says, except in some instances of proved disorders of the thyroid, pituitary or sex glands, in which case application of hormone preparations may be of some help.

As a solution of the problem of the depleted pate, the writer suggests that we concentrate not so much on cures for baldness, but on establishing "a new philosophy of hair" in which its cosmetic importance is played down much more than at present.

And, oh yes, if you have nothing to do on a rainy day, Miss Sheppard suggests that you try to count the hairs on your head, if any. If you're a blond, you'll find you have around 140,000 while if you're a brunette, you'll average only about 100,000.

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FAVORABLE RESULTS OF SURGERY ON "BLUE BABIES" REPORTED

"Tremendous improvement" in the condition of 39 children who underwent heart surgery to relieve the so-called "blue baby" condition is reported by Willis J. Potts, M.D., and Stanley Gibson, M.D., of Children's Memorial Hospital, Chicago.

Writing in the current issue of *The Journal of the American Medical Association*, they say that "of 41 patients who have survived surgery, 39 have been tremendously improved; i.e., they are relieved of cyanosis, have gained weight and are able to live fairly normal lives."

The surgical procedure discussed by Drs. Potts and Gibson was first reported by them, and by Sidney Smith, M.D., Chicago, in the Nov. 16, 1946 issue of *The Journal of the A.M.A.* after the operation had been performed successfully on two children.

The "blue baby" is characterized by bluish fingernails, clubbed finger tips, purple lips, a bluish complexion and bloodshot eyes. The condition arises when the malformed heart cannot pump enough blood to the patient's lungs to pick up the vital oxygen which the body needs.

The operation described by Drs. Potts and Gibson is designed to increase the oxygenation of the blood stream by increasing circulation through the heart.

As described by Drs. Potts and Gibson in the current issue of *The Journal*, the procedure remains substantially the same as that outlined in the Nov. 16, 1946 issue, except for "slight modifications in technic" and "clarification of misunderstood points."

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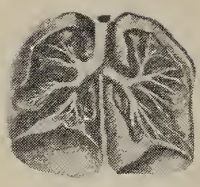
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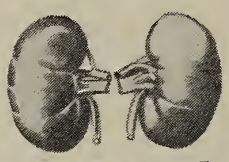
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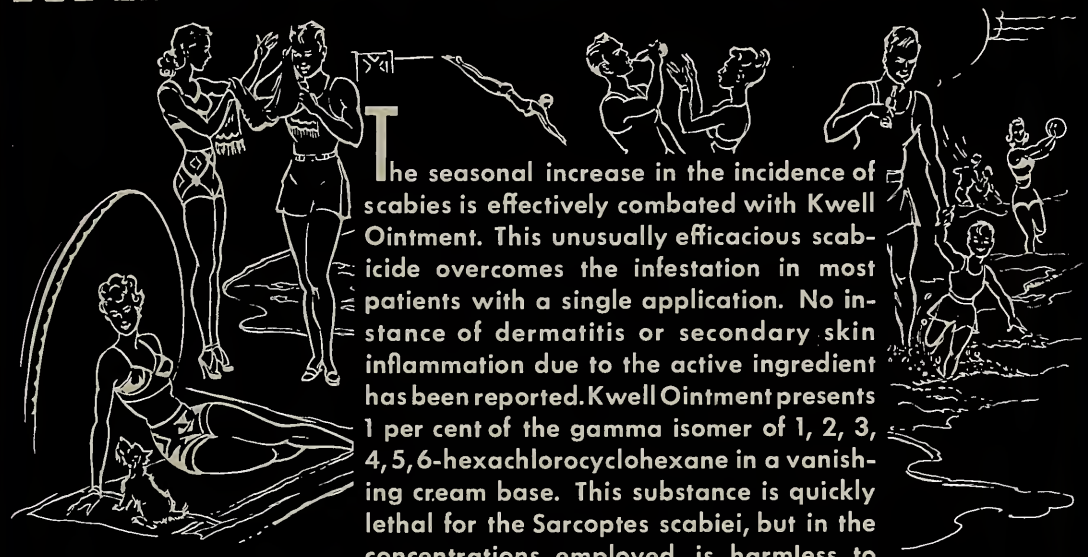
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LIVING COSTS RISE FASTER THAN PHYSICIANS' FEES

The cost of living has risen more rapidly than the fees charged by physicians for medical services, according to Frank G. Dickinson, Ph.D., director of the Bureau of Medical Economic Research of the American Medical Association.

In his new study entitled "Comparative Increases in the Costs of Medical Care and the Costs of Living," Dr. Dickinson stated that the quantity of medical care received by the American people was at least two-thirds more in 1946 than in 1939.

"When the various indexes and ratios are studied," Dr. Dickinson said, "it can be seen that the quantity of medical care received by the American people has probably increased much faster than the increase in the number of physicians. This apparent 'output' per physician doubtless reflects the increasing use of technical assistants.

"Whether one examines the record of total expenditures of the American people for medical care or the prices of significant items during recent years, he comes to the general conclusion that the American people have been fortunate in that the costs of keeping well have not risen as rapidly as the cost of living."

In his new study, just off the press, Dr. Dickinson made extensive use of the price indexes compiled by the U. S. Bureau of Labor Statistics. A four-page bulletin contains figures and charts supporting his conclusions.

The Bureau of Labor Statistics index, covering cost of living in 34 cities, was 59 per cent higher in 1947 than in the base period of 1935-39.

The Bureau's 1947 index for all medical care, including drugs, was only 32 per cent above the 1935-39 period. Excluding drugs, the increase was 35 per cent and for drugs only the increase was 15 per cent.

"This doesn't reflect the quantity of medical care," Dr. Dickinson said, explaining that the 1946 index of personal consumer expenditures for medical care was 211, or 111 per cent above the 1935-39 base period.

"A statistician," he explained, "arrives at the index of quantity of medical care by dividing the index of expenditures by the index of prices of medical care." Thus, he established that the index of expenditures for 1946, 211, was more than two-thirds higher than the index of prices of medical care, 122.

He used the index of personal consumer expenditures for all medical care items as provided by the U. S. Department of Commerce.

Dr. Dickinson estimated that the quantity of physicians' services—one of the medical care items—was approximately one-half greater in 1946 than in the base period 1935-39, but the number of physicians was only one-seventh greater.

Dr. Dickinson's newest study is the second made within a year. In 1947, he published a study entitled "Is Medical Care Expensive?" In this 12-page pamphlet, Dr. Dickinson said that medical care items as a whole cost the American people $5,600,000,000 in 1946, but that only 3.9 per cent of the

(Continued on Page 22)

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LIVING COSTS RISE FASTER THAN PHYSICIANS' FEES

(Continued from Page 20)

total personal consumer expenditures of the American people were spent for these medical care items. This compared with 4.3 per cent in 1940.

He also found in his first study that in 1946 physicians received only 26 per cent of all the dollars spent for medical care as compared with 31 per cent in the base period, 1935-39, and 32 per cent in 1929, the first year for which the data were gathered and published by the U. S. Department of Commerce. On the other hand, he found that the amount spent for drugs in 1946 had risen to 24 per cent of all dollars spent for medical care as compared with only 21 per cent in the base period, 1935-39, and 20 per cent in 1929.

PHYSICAL MEDICINE USED SUCCESSFULLY IN PARALYSIS

Marked success in the treatment of hemiplegia, which is a paralysis of one side of the body due to brain hemorrhage, through the use of physical medicine is reported by Comdr. Edward W. Lowman (MC), U.S.N., of the Department of Physical Medicine, U. S. Naval Hospital, Philadelphia.

Physical medicine includes the employment of the physical and other effective properties of ultraviolet and infra-red rays, the use of heat, cold, water, electricity, massage, manipulation, exercise and mechanical devices for diagnosis and treatment of disease.

Writing in a recent issue of *The Journal of the*

(Continued on Page 26)

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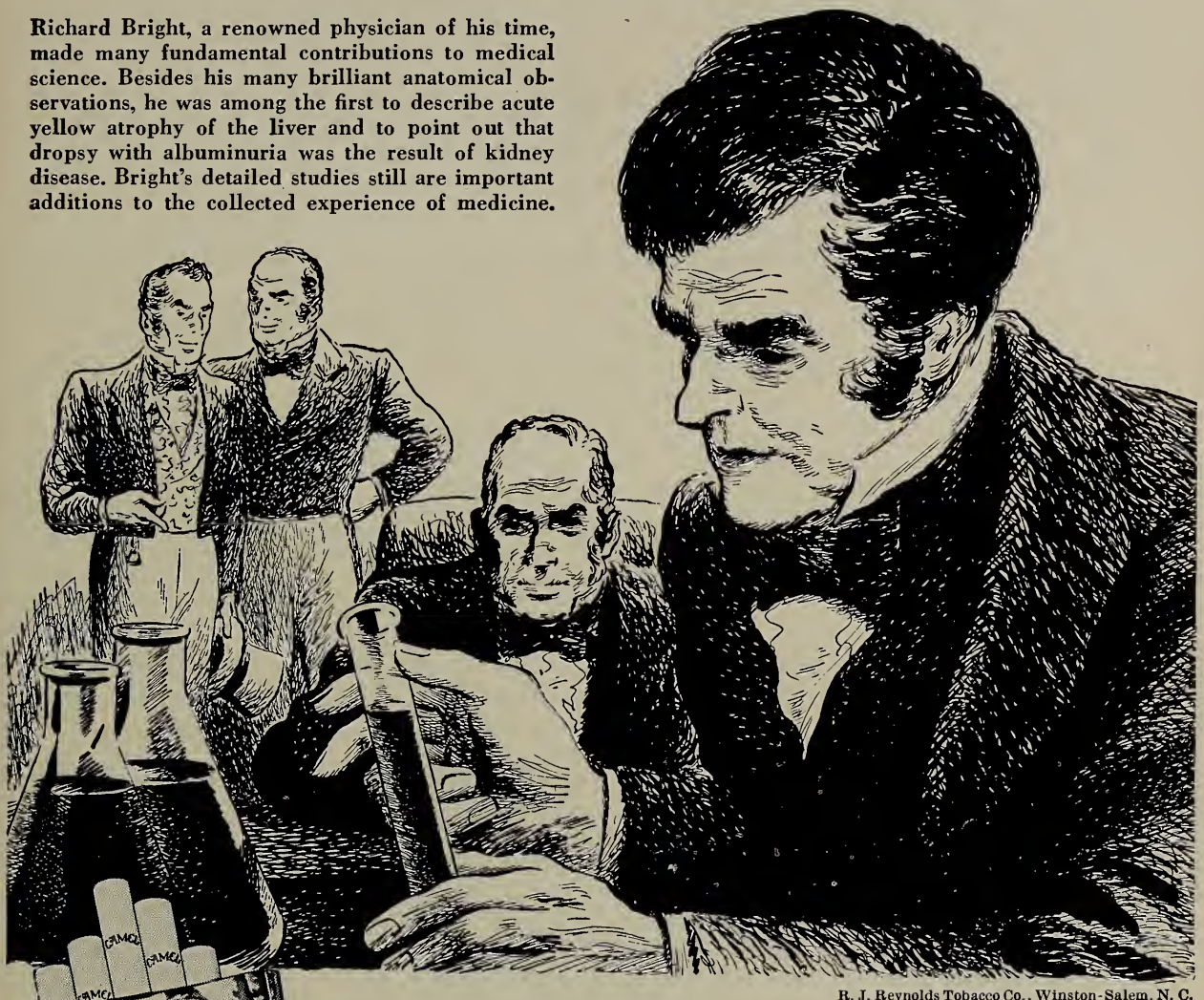
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PHYSICAL MEDICINE USED SUCCESSFULLY IN PARALYSIS

(Continued from Page 22)

American Medical Association, Comdr. Lowman reports that out of 18 chronic cases of paralysis due to brain hemorrhage, 12 learned to walk again after undergoing an intense program of physical medicine for 118 days, while three showed definite improvement. There was no improvement in the condition of the remaining three.

In 10 additional new cases, nine of the patients learned to walk again after 67 days of treatment, and improvement was noted in the other patient.

Commenting on the results of the treatment, Commander Lowman says that "the early, intensive and intelligent use of physical medicine, with emphasis on therapeutic reconditioning exercises, assures a potentially good prognosis in the rehabilitation of patients with uncomplicated hemiplegia."

The program of rehabilitation employed by the Navy doctor was begun from two to four weeks after the onset of the acute illness.

The first stages included massage, application of heat and therapeutic baths, followed by active exercises in bed when voluntary motion was possible.

Efforts to learn to walk again were begun early, usually within two to eight weeks after treatment was started. This was a gradual process, beginning with sitting up in bed and placing the feet on the floor from the bedside, and concluding with exercises in the gymnasium.

(Continued on Page 28)

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PHYSICAL MEDICINE USED SUCCESSFULLY IN PARALYSIS

(Continued from Page 26)

The gymnastic program, which was conducted under the supervision of a trained physical therapist, consisted at first of simple mat exercises and ultimately of more difficult ones on bars, stationary bicycles and other devices.

This program varied somewhat for each patient, depending on his physical and mental condition.

According to Comdr. Lowman, the greatest factor in the success of the rehabilitation treatment is "cooperation on the part of the patient, fostered by his desire to regain his independence."

SEAT NEXT TO DRIVER CALLED MOST DANGEROUS

Automobile passengers occupying the front seat next to the driver are in the most dangerous position in the car, according to a Detroit plastic surgeon writing in a recent issue of *The Journal of the American Medical Association.*

In his report, Claire L. Straith, M.D., chief of the Plastic Surgery Division, Harper Hospital, Detroit, says:

"Drivers occupy the safest seat in the car; protected by the steering wheel, they escape injury in many severe accidents. 'Guest passengers' in the front seat beside the driver are, on the contrary, in

(Continued on Page 30)



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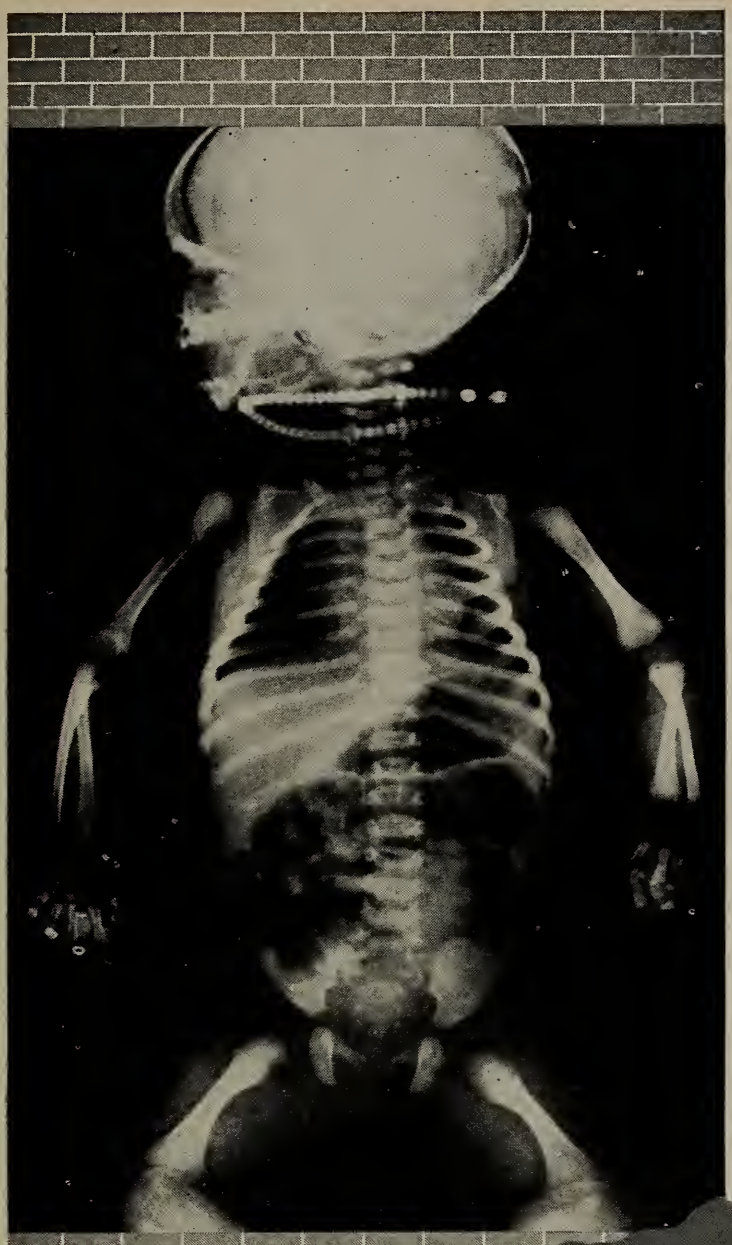
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SEAT NEXT TO DRIVER CALLED MOST DANGEROUS

(Continued from Page 28)

the most dangerous seat in the car because of their unprotected position in case of sudden stops."

According to the article, occupants of the "death seat" beside the driver are injured at the rate of about three to one, as compared to the driver. In a study of 50 consecutive patients with facial injuries from automobile accidents, Dr. Straith discovered that about 70 per cent were young women and girls who had been riding in the front seat next to the driver.

Substantiating his "death seat" theory, the Detroit surgeon cites figures secured from the Detroit police department, showing that in 219 accidents involving multiple occupants, 260 passengers but no drivers were injured.

According to the article, the Detroit study showed that more than half of those front seat passengers involved in auto accidents sustained injuries of the head, including facial cuts and damage to the teeth, chin, nose, cheeks, ears, forehead and skull.

Among the remedies suggested by the writer to reduce the "death seat" danger are removal of all knobs, cranks, drop down ash trays and sharp ledges from the dash board and the use of rubber padding on the dash in front of the guest passenger.

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Q Fever in Artesia, California

FRANK W. YOUNG, M.D., *Artesia*

IN the area around Artesia, California, a region of about 12,000 population in southeastern Los Angeles County where dairying is a principal industry, outbreaks of fever in humans were noted following arid spells and windstorms last year. These outbreaks, which followed with almost predictable regularity and within four or five days after the so-called Santa Ana windstorms, were ascribed variously to influenza, virus pneumonia, primary atypical pneumonia, and infection of unknown origin. The salient clinical features were severe and persistent headaches, fever with little matinal remission, rigors, generalized malaise and occasionally pneumonia with a paucity of clinical findings as confirmation.

The similarity of conditions in Artesia to those in Amarillo, Texas, where the epidemic of 1946 caused nation wide interest, suggested the possibility of Q fever, and for this reason blood from 14 patients was sent to the National Institute of Health in Bethesda, Maryland. Reports on eight were returned strongly positive for Q fever. In these cases the patients' temperature returned to normal in from one to three weeks. One of the remaining blood specimens was slightly positive and five were negative. (It should be noted that the negative report on those five patients, who had acute symptoms, is not conclusive, since the complement fixation test does not develop a positive reaction in the acute states of the disease.)

The fact that there was positive reaction in eight of the fourteen specimens of blood permits assumption of a clinical diagnosis of Q fever in 20 or 30 similar cases in which the patients' blood was not tested but in whom the onset and course were similar.

CLINICAL DATA

Figures 1 and 2 are roentgenograms of the chests of two patients hospitalized, and these films were diagnosed by the roentgenologist as characteristic of primary atypical pneumonia.

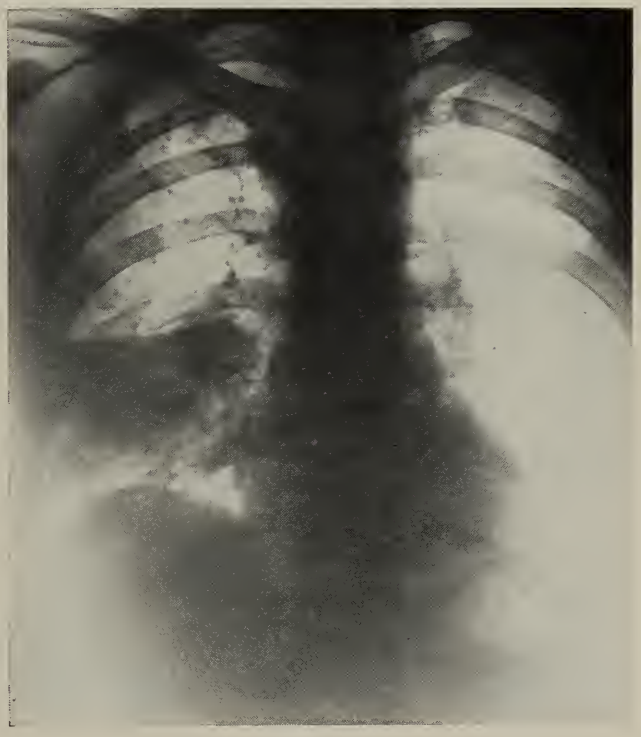


Figure 1

Blood-tinged sputum was observed in several cases, including the two in which the patients were hospitalized, and without exception in those patients in whom the course of the disease was prolonged. It is reasonable to assume pneumonic infiltration in the patients who were not hospitalized.

The erythrocyte count, hemoglobin determination and leukocyte count all were essentially within normal range. Albumin and granular casts were observed in the urine of a few patients in whom the febrile course was unusually stormy.

The fever ranged from 101° to 105° F. with little remission in the severe cases, and the intensity of headache and malaise paralleled the febrile course.



Figure 2

Headache was bitterly complained by most of the patients. After convalescence, however, the discomfort was seldom remembered. This observation has been corroborated by Dr. Charles S. Shepard of the rickettsial research unit of the National Institute of Health. This amnesia for the discomforts experienced during the stormy course of the disease would suggest possible encephalitic cellular changes.

Spinal fluid examination was not done in any case but a thorough examination of the nervous system disclosed no abnormalities.

Treatment in all cases consisted of penicillin injections, 200,000 units daily, with sulfadiazine by mouth, 6 gm. daily in divided doses. This combination seemed to have a salutary effect, but evaluation of it was difficult because of the marked variance in the course of the disease.

In the cases not complicated by pneumonic invasion the patients usually were afebrile in three to seven days. In a few instances morphine sulphate hypodermically in doses of 0.03 gm. (Gr. 0.5) was necessary to alleviate discomfort. Para-aminobenzic acid was not used.

COMMENTS

All reported cases of Q fever which occurred during the explosive outbreak in March in Amarillo, Texas, were among workers in three places associated with the handling of live stock. In Artesia and its environs the cases were catholic in distribution. One positive reaction to the complement fixation test was obtained in the blood of a ten year old schoolgirl, another in blood of a fourteen year old high school freshman, and still another in blood from a housewife whose husband was a mechanic in a garage.

The fact that definitely proved cases of Q fever followed so closely upon dust storms in the Artesia area would seem to question the accepted proposition that the incubation period of the disease is 14 to 26 days. It is the author's opinion that Q fever is much more prevalent than hitherto believed. Also, it is suggested that *rickettsia burneti* is indigenous to dust in the vinicity of cattle barns and corrals, and is disseminated by winds following arid spells. These atmospheric conditions existed in Artesia immediately before outbreak of the epidemic. The opinion is expressed that the disease may be contracted without direct contact with cattle.

1442 Pioneer Boulevard.

Q Fever in California

Edwin H. Lennette, Ph.D., M.D., *Berkeley*

In 1935 there occurred among packing house workers in Brisbane, Australia, a number of cases of an obscure febrile illness. Derrick,[15] who investigated the outbreak, recognized that it represented a disease previously undescribed, and tentatively named it "Q"* fever, the name by which it is still known. This new entity was found to belong to the rickettsioses[5] and the causal agent was designated[16] as *Rickettsia burneti* (now known as *Coxiella burneti;* vide infra).

Meanwhile, in the United States a filtrable agent was isolated by Davis and Cox[13] (1935) from ticks *(Dermacentor andersoni)* collected in the Nine Mile Creek area, about 30 miles west of Missoula, Montana. The agent was identified as a rickettsia and because, unlike other members of this group, it was readily filtrable, it was named *Rickettsia diaporica.*[11] Its role, if any, in the causation of human disease was unknown, but its pathogenicity for man was subsequently revealed when an accidental laboratory infection occurred.[19] Laboratory studies on this case suggested[19] that the infection was related to Australian Q fever; later, detailed immunologic investigations[2, 6, 20] proved that *R. burneti* and *R. diaporica* are essentially identical, and that the "Nine Mile fever" of Montana and the Q fever of Australia are the same disease.

Until 1944, Q fever was considered to be a disease confined to Australia and the United States. Then, between November, 1944, and June, 1945, there occurred eight outbreaks, totaling approximately 600 cases, among allied troops stationed in Northern Italy, Greece and Corsica.[31] In addition, there was an explosive outbreak involving approximately one-third of a group of 1,600 troops returning to this country from Southern Italy.[8]

Q fever was reported from Panama[7] in 1946 and from Switzerland in 1947.[22]

Prior to 1946 naturally acquired Q fever appeared to be rare in the United States. Several outbreaks of atypical pneumonia studied prior to 1944 gave no evidence that *R. burneti* was involved,[17, 38] and the only authentic case was that described by Hesdorffer and Duffalo[23] in Montana (1941). The probability that the disease may be widespread, however, had been suggested by Cox,[12] who found specific antibodies in the sera and/or isolated the rickettsia from 19 patients from Idaho, Montana, Wyoming, Nebraska, Nevada, Oregon, and Washington.

From the Viral and Rickettsial Disease Laboratory, California State Department of Public Health, 1392 University Avenue, Berkeley 2, California.

Read before the sections on Public Health and General Practice at the 77th Annual Session of the California Medical Association in San Francisco, April 11-14, 1948.

*According to a personal communication from Dr. Derrick, the "Q" stands for "query" rather than "Queensland."

In March, 1946, the first known naturally occurring outbreak of Q fever in this country appeared explosively at Amarillo, Texas, when 55 cases, with two deaths, occurred among the 136 employees of three packing houses.[36] In August of the same year another outbreak occurred, this time at a Chicago packing house where 33 of 81 men on a killing floor were affected.[34]

In May, 1947, the presence of the disease in California was uncovered by Dr. Frank Young of Artesia, who suspected that some of the unusual pneumonias he was encountering might be due to *R. burneti.* (See page 89, this issue.) Serologic tests at the National Institute of Health confirmed his clinical impressions, and a rapid survey made by the United States Public Health Service revealed that the disease is endemic in Southern California. A field laboratory for the study of the epidemiology of Q fever was established at Hondo on the property of the Rancho Los Amigos, and staffed with personnel from the United States Public Health Service and the California State Department of Public Health. The investigation is a joint project of the National Institute of Health, the California State Department of Public Health, the Los Angeles City and County Health Departments, and the California State Department of Agriculture.

ETIOLOGY

The causal agent of Q fever is, as already mentioned, a rickettsia which etiologically, therefore, places this disease in the group to which belong epidemic and murine typhus, scrub typhus, Rocky Mountain spotted fever, boutonneuse fever, and the newly described rickettsialpox. Morphologically and tinctorially, *Rickettsia burneti* resembles the other rickettsiae, but it is of interest that in certain other respects it differs from them. Thus, the organism is filtrable;[5, 11] it forms large microcolonies (strikingly similar to those seen with psittacosis virus) in infected cells in the mouse spleen;[5, 9] it produces no soluble antigen,[37] nor does it produce agglutinins to the "X" strains (OXK, OX2, and OX19) of *B. proteus;*[5, 12, 15] also, the rash seen with other rickettsial diseases is absent in Q fever.

Because of these striking characteristics which set off the Q fever organism from the other rickettsiae, it was proposed by Bengtson, Steinhaus, and others (see, for example, Philip[30]), that the organism be placed in a new genus to be known as Coxiella, the genotype to remain the same. This has been accepted and *Rickettsia burneti* Derrick now becomes *Coxiella burneti* (Derrick), and is so listed in the latest (1948) edition of Bergey's Manual of Determinative Bacteriology.[3] The new terminology, therefore, will be used from this point on in the present discussion.

CLINICAL ASPECTS OF Q FEVER

Onset.—The incubation period is from 14 to 32 days,[31,34] with an average of about three weeks. The onset may be abrupt,[32] or may be gradual,[21] the proportion of cases in either category varying with the outbreak. In general, the illness appears to be more severe if onset is sudden.

The initial symptoms are predominantly constitutional and there are few or no symptoms referable to the respiratory tract. Presenting complaints are headache, feverishness, sweats, chilly sensations, muscular aches, chest pain, tiredness, and anorexia.

Symptoms.—Headache, frontal or occipital, is the most frequent symptom; it varies greatly in severity but generally is one of the major complaints. Chilly sensations are common, but true rigor is seldom seen.[21, 32] Generalized malaise is frequent, as are muscular aches and pains; the latter may be quite marked and if in the nuchal area may lead to a suspicion of meningitis. Retro-orbital pain is also a common complaint. Photophobia may occur, but is rare. Anorexia of variable degree is encountered during the febrile stage, and nausea and vomiting are present in some cases.

Respiratory symptoms such as nasal stuffiness or discharge, sore throat, and sneezing, are generally minimal, if present. Cough also may be absent, but generally appears about the fifth day and is slight and dry; in about one-third of the cases the cough is productive.

Chest pain occurs in one-third to one-half of the patients; it may be mild, brought about by deep inspiration or coughing, may be a dull ache or a feeling of oppression in the chest or, occasionally may be a true pleuritic pain.

Physical findings.—The physical signs in Q fever, as in the so-called atypical pneumonias of viral origin, are few.

There is fever ranging from 101°F to 105°F, and the patient is flushed and appears acutely ill. The nasal and pharyngeal mucous membranes may be injected or congested, but this is seldom marked. The pulse rate rises with the temperature, but there is a relative bradycardia. The respiratory rate is normal.

Abnormal physical signs in the chest may be present, but are seldom very obvious. Slight diminutions in breath or voice sounds, decreased tactile fremitus, and friction rub occasionally may be detected, and there may be some localized dullness over a pneumonic area. Coarse rales or rhonchi are unusual. Most frequently encountered are very fine crepitant rales, heard best at the end of deep inspiration. These are usually transient, persisting for only a day or two, and so may be missed unless looked for; in some instances they are present over a period of a week or more.

Course.—The disease is variable in severity and there is little correlation between severity and the amount of pulmonary involvement. The temperature returns to normal within a seven to ten day period on the average. With defervescence, the symptoms disappear in the moderately ill, but weakness and fatigue on slight exertion may persist for several weeks in those with a severe attack. Some loss in weight occurs in the more severe cases. Relapses have been described.[18]

Clinico-pathologic findings. — The erythrocyte count and hemoglobin concentration are normal. Leukocyte counts are normal or a little low, ranging from 4,000 to 10,000. The blood sedimentation rate is increased during the symptomatic period and returns to normal when the patient is asymptomatic. Results of urine examinations are negative.

Roentgenologic studies of the chest almost always reveal the presence of some patchy consolidation, usually involving only one lobe, but sometimes more. The lower lobes are the most frequently affected, but any lobe may be involved. The lesions appear on the third or fourth day, are located peripherally and have a homogeneous, ground-glass appearance. They increase in size by extension to reach the maximum at about the time the patient becomes afebrile (seven to ten days), then regress slowly, sometimes persisting for days after the patient has otherwise completely recovered.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The symptoms in the early stages of Q fever are no different than those encountered in many other febrile conditions and afford no means of distinguishing this disease from others such as influenza, brucellosis, the enteric fevers, and meningitis, to mention only several; the usual laboratory examinations also provide no assistance.

Pulmonary involvement may later be suspected from the physical findings, but is best demonstrated, or confirmed, by roentgenograms of the chest. The presence of pneumonitis leads generally to a diagnosis of "atypical pneumonia," which, it might be pointed out, is a clinical syndrome, not a disease entity with a specific etiology. If a definite diagnosis based on etiology is to be achieved, consideration must be given at this stage to the diverse agents which can produce this picture. Among these, in addition to the Q fever rickettsia, are various bacteria (pneumococcus, streptococcus, staphylococcus, Friedlander's bacillus, tubercle bacillus) the fungi (Monilia *sp.*, and *Coccidioides immitis*), and the viruses of influenza, lymphocytic choriomeningitis, and especially those of psittacosis and ornithosis. (There exists, however, a large residuum of cases in which the specific cause of the pneumonitis cannot be resolved;* these have been classified by the Army Commission[18] as "primary atypical pneumonia, etiology unknown," and it is in this group that the cold hemagglutination phenomenon is encountered.)

The bacterial pneumonias are differentiated by leukocytosis, presence of specific organisms in the

*Eaton and his associates (see the excellent review by Meiklejohn[25]) have presented evidence, however, that more than one-half of the cases in this category are due to a virus which they have isolated on a number of occasions and to which the patients develop neutralizing antibodies.

sputum, and response to chemotherapeutic or antibiotic agents.

A fungal factor in the etiology is demonstrated by the presence of the fungus in the sputum, and in the case of coccidioidomycosis, by serological and skin tests.

Influenza is associated with upper respiratory disease symptoms, but isolation of the virus or serological tests are required for absolute certainty.

Cases due to the virus of lymphocytic choriomeningitis or those of the psittacosis group are diagnosed by serologic methods, or by isolation of the specific virus from sputum or blood, or from tissues postmortem. A history of contact with birds may point to psittacosis or ornithosis, but the diagnosis should be confirmed by laboratory methods.

A definitive diagnosis of Q fever is made by isolation of the rickettsia through inoculation of blood into guinea pigs or by showing that complement-fixing antibodies develop during the illness. *It should be emphasized here that for the serological diagnosis of rickettsial and viral diseases, two specimens of blood, one taken in the early, acute stage of the illness and a second taken later in the convalescent phase, are required since diagnosis depends upon the demonstration of the appearance or rise in titer of specific antibodies.* Agglutinins to the X strains of *B. proteus* are not evoked in this disease, and hence the Weil-Felix test is of no aid in diagnosis.

TREATMENT

Therapy is entirely symptomatic and supportive. Sulfonamides and penicillin have no effect on the course of the disease. Streptomycin has been reported[25] to lower the mortality rate of guinea pigs inoculated with *Coxiella burneti*, but its usefulness in human infections is unknown.

EPIDEMIOLOGY

With the discovery that Q fever is a rickettsial disease, and with the knowledge that the other rickettsioses are transmitted by arthropods, a search early was made for possible arthropod vectors of this disease. The occurrence of naturally-infected ticks has been reported from Australia *(Haemaphysalis humerosa)*;[35] the United States *(Dermacentor andersoni* (Montana[13] and Wyoming[14]) *D. occidentalis* (West Coast States[27]) and *Amblyomma americanum* (Texas[29])); and Morocco *(Hyalomma savignyi)*,[4] but clinical and epidemiologic studies have failed to incriminate this arthropod, or any other, in the transmission of Q fever to man.

The work of the Australian investigators indicates that Q fever is primarily an infection of bandicoots (a small marsupial) and cattle, among which it is disseminated by ticks; the human disease represents only accidental infections, arising outside, and not necessary to, the maintenance of the basic cycle, and presumably is acquired by inhalation of dried tick excreta on the hides of cattle. This would explain the high incidence of the disease in those whose occupation brings them into contact with cattle, and seems to be the only explanation for the cause of such outbreaks as that at Amarillo. Similarly, in the Italian outbreaks, dust, either that in the quarters as a whole or from hay and straw used for bedding, appeared to be the most likely source of infection; since various birds and animals shared the buildings with the human tenants, it is not impossible that the dust was contaminated with excreta from infected birds or animals or their ectoparasites. Finally, the only logical explanation for the several laboratory outbreaks[10,24,33] is that the agent was air-borne. Person-to-person transmission apparently does not occur.[31]

Epidemiologic studies initiated in Los Angeles County by Shepard and Huebner of the National Institute of Health following the discovery of the disease in that area indicated that many cases were in persons occupationally associated with cattle (livestock handlers, dairy workers). Serologic studies on cattle revealed that many possessed antibodies to *Coxiella burneti*—e.g., 12.5 per cent of 1050 animals in one herd, approximately 30 per cent of 90 animals in another[26]—indicating that these animals had been or were infected. Inoculation into guinea pigs of single or composite milk samples pooled from random strings of cows gave evidence that 40 of the 50 specimens tested were infected,[26] a remarkably high proportion. Since, according to serologic surveys, infection is geographically widespread among the cattle population, and as the milk, much of it raw, is widely distributed in the same area, some relationship between these factors and human infection is suggested. Ingestion of infected milk has been tentatively considered as a possible cause of the human disease, but the evidence thus far is not conclusive, first because of insufficiency of data and, second, because of findings that in certain groups of individuals this mode of transmission was improbable. On the other hand, it remains to be proved that infected milk plays no role in the epidemiology of the disease —infection may be acquired through some route other than the oral.

To date, approximately 200 cases of Q fever have been diagnosed in California. Practically all have been in Los Angeles County, but single cases have been diagnosed serologically in Santa Barbara, Ventura, and Orange counties.

At the present stage of the study, there is no indication of seasonal differences in the occurrence of cases, but a much longer interval of observation is necessary before a valid judgment can be reached. The age of the patients ranged from 3 to 75 years,[1] the majority coming within the 20-44 year old group. Males were affected more frequently than females, the ratio being 4 to 1.[1] Both the age and sex distribution, however, presumably will have to be revised as more information is acquired, since the present figures are derived in large part from certain groups with occupational exposure to livestock (packing houses and dairies).

The Viral and Rickettsial Disease Laboratory of the California State Department of Public Health has just recently demonstrated the presence of antibodies to *C. burneti* in the convalescent sera of four individuals residing in Northern California (Solano,

Yolo, Glenn, and Plumas counties), and giving a history of a recent febrile illness. In addition, a clinical case of Q fever in a patient in Stanislaus County was investigated, and serologic studies disclosed that all the six other members of the patient's family also possessed Q fever antibodies. There has been no opportunity as yet to investigate epidemiologically any but the Stanislaus County cases. In these, it was possible to rule out exposure to the disease in Southern California, and it appears that infection was acquired locally. It is of interest that while only 1 of 26 cattle on the ranch possessed demonstrable antibodies to *C. burneti,* antibodies were present in 12 of 30 goats tested. Inasmuch as the cattle herd is essentially a closed one, and is serologically negative, suspicion at present is centered on the goats, not only because of the high percentage with antibodies, but also because several acute illnesses, one quite severe, occurred in members of two families quartered on the ranch within several weeks after the goats were introduced there.

SUMMARY

Q fever has now been shown to occur in California, and the probability exists that more cases will be encountered. The presence of the disease requires that it be considered in the differential diagnosis of acute febrile illnesses as well as of the so-called viral pneumonias. Definitive diagnosis, however, rests on isolation of the rickettsia through inoculation of the patient's blood into guinea pigs, or by examination of paired serum specimens for the appearance, or rise in titer, of specific antibodies to *Coxiella burneti.*

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Primary Carcinoma of the Lung

Diagnosis by Cytological Studies of Sputum and Bronchial Secretions

Seymour M. Farber, M.D., Mortimer A. Benioff, M.D., and
Gerd Tobias, M.D., *San Francisco*

A RECENT study of 200 cases of primary carcinoma of the lung that came to autopsy[2, 3] revealed that the diagnosis usually had been made in the late stages of the disease or at autopsy. This late diagnosis of a disease which annually results in over 15,000 deaths in the United States is regrettable since thoracic surgeons are now able to remove the involved lung with "cure" in many cases if the diagnosis is established early. Consequently, attention should be centered on the early diagnosis of this disease.

The most important single factor in the diagnosis is that the physician must think of the possibility of bronchogenic carcinoma. Among the more common early respiratory symptoms are persistent cough, hemoptysis, pain in the chest and wheezing. Cough is relatively dry at first and is more productive later. Symptoms of this nature occurring in a patient, particularly in a male over 40 years of age, should immediately suggest the possibility of bronchogenic carcinoma. If the presence of this disease is suspected a thorough course of investigation should be carried out. This should include the taking of a careful history, physical examination, complete roentgenological study of the chest, and bronchoscopy. Lipiodol studies may be helpful. Often exploratory thoracotomy is necessary to establish the diagnosis.

Attention has been focused recently on a simple method of suggesting, establishing or confirming the diagnosis of primary carcinoma of the lung. Inasmuch as primary carcinoma of the lung is considered bronchogenic and the malignant cells tend to exfoliate into the lumen of the bronchus, it is logical to attempt to find these free cells in the sputum or bronchial secretions. It is the purpose of this paper to discuss some of the more important features of this diagnostic method.

From the University of California Medical Service, San Francisco Hospital and the San Francisco Department of Public Health.

HISTORY

The presence of neoplastic cells in the sputum of a patient with bronchogenic carcinoma was first reported by Hampeln in 1887.[4] Hampeln and other early workers prepared sputum for microscopic examination in dried smears or imbedded histological sections which were usually stained by simple methods. Unlike the earlier workers, Dudgeon and Wrigley in 1935 used wet films which they fixed in Schaudinn's fluid and stained with Meyer's hemalum and eosin.[1] In 1944 Wandall in Denmark reported finding neoplastic cells in the sputum by using a wet film technique and staining with hematoxyln and eosin.[9] Herbut and Clerf reported on the adaptation to the study of bronchial secretions of the Papanicolaou technique for studying vaginal cytology.[5] Numerous other reports have appeared in the English, Latin-American and Russian literature.

METHOD OF PREPARING SLIDES

Material must be carefully obtained and slides properly prepared in order to preserve the cytologic detail essential for the recognition of malignant cells and differentiation of them from the normal cellular flora of sputum or bronchial secretions. If sputum is to be examined the patient is instructed to raise secretions from the lower part of the respiratory tree. Smears should be made immediately to avoid loss of cellular detail by autolysis. If there is to be a period of time before slides are prepared and fixed, it is best to have the sputum expectorated into jars containing 10 cc. of the fixative solution. Sputum should

be examined in a Petri dish against a dark background. Various suspicious components of the sputum such as tissue fragments or blood flecks are selected, using a magnifying glass if necessary, and are gently smeared over two-thirds of the slide. Pressure will cause distortion during this procedure. Thick smears are not suitable for the study of cytologic detail. It is important to immerse the smears in the fixative solution while they are still wet. This fixative solution consists of equal parts of ether and 95 per cent ethyl alcohol. A paper clip attached to alternate slides will separate the smears.

Bronchial secretions obtained at bronchoscopy are treated in the same manner. Secretions should be obtained from suspicious areas of the bronchial tree for preparation of slides. If secretions are very scant all material should be saved.

We have found that after fixation for a two-hour period slides may be removed from the solution and permitted to stand, protected from dust, for at least seven days before staining. This permits mailing of slides to laboratories where trained personnel can examine the smears.

Smears are stained by the Papanicolaou technique. This method has been described in detail in the monograph of Papanicolaou and Traut on the diagnosis of uterine cancer by the vaginal smear.[8] It is not necessary with this technique to control the nuclear stain with microscopic observation as it is with hematoxyln and eosin.

CYTOLOGY OF SPUTUM AND BRONCHIAL SECRETIONS

Nonmalignant components. The nonmalignant components of sputum and bronchial secretions are epithelial cells, cells from the blood and cells from the reticulo-endothelial system. Epithelial cells include ciliated columnar cells from the trachea and bronchi. Squamous cells originate in the mouth, pharynx and, occasionally, in areas of metaplasia in the lower part of the respiratory tree. Blood elements which may be observed include erythrocytes, polymorphonuclear leukocytes, lymphocytes, monocytes and, occasionally, megakaryocytes. The reticulo-endothelial system contributes macrophages (histiocytes) and giant cells. Macrophages may exhibit marked pleomorphism. They may be mistaken for malignant cells, particularly when they do not contain phagocytised particles. A careful and thorough study of sputum from patients suffering from various types of nonmalignant respiratory disease is a necessary prerequisite to study of smears for neoplastic cells.

Malignant components. Neoplastic cells found in the sputum and bronchial secretions may be classified as differentiated and undifferentiated. Differentiated neoplasms in the lung include squamous cell (epidermoid) carcinomas and adenocarcinomas. It is not always possible to assign one malignant cell to the appropriate classification when it is encountered alone. When groups of malignant cells are seen it may be possible to classify them. The average malignant cell usually is large but it may not be, particularly if it is exfoliated from anaplastic carcinomas. The nuclear-cytoplasmic ratio is usually large and at times the nucleus may appear to be naked. The nuclei may attain excessive size. They can vary in shape, position and size, and one cell may have more than one nucleus. This variability is particularly noted when various malignant cells are compared. The chromatin is usually arranged in irregular fragments or in a coarse meshwork. Mitotic figures may be observed. Nucleoli vary in size, shape and number from one cell to another. Groups of malignant cells may be crowded together in a manner not seen in macrophages or other normal cellular components. Phagocytosis is rarely exhibited by malignant cells.

RESULTS OF CYTOLOGIC STUDIES

Wandall reported finding neoplastic cells in the sputum of 84 of 100 cases of bronchogenic carcinoma. Herbut and Clerf preferred to work with secretions aspirated at bronchoscopy because the specimen was less diluted with secretions from upper portions of the bronchial tree. They reported malignant cells in 46 of 57 (89 per cent) cases of proven bronchogenic carcinoma. Woolner and McDonald[10] reported that they were able to demonstrate neoplastic cells in 70 cases, but it is not clear in how many of their cases the diagnosis was substantiated by tissue studies nor in what percentage of proved bronchogenic carcinoma the smears were positive.

We have used this diagnostic method for 15 months, and cytologic study of 1,512 specimens from 414 patients suspected of having "carcinoma of the lung" has been carried out. Positive or suspicious cells were found in 69 cases. Pathologic confirmation of the diagnosis of carcinoma of the lung has been established in 56 cases. In 46 (82 per cent) of these 56 cases, cytologic examination revealed or suggested the presence of bronchogenic carcinoma. Sputum smears were obtained in 52 cases of proved malignant disease; in 43 (82 per cent) of these cells were found which indicated or suggested the diagnosis of carcinoma of the lung.

As diagnostic criteria were developed and perfected our efficiency improved. As with any technique many of the early mistakes were found to be avoidable. We feel that diagnostic efficiency will be increased as a result of additional experience in evaluating the appearance of malignant, as well as the normal, components of the sputum.

REPORT OF THREE CASES

Three cases in which malignant cells were demonstrated in the sputum and the diagnosis was later confirmed by tissue examinations, are presented.

Case 1.—A white man 67 years old was hospitalized on July 31, 1947. He complained of malaise, loss of weight, difficulty with breathing and a productive cough of four months' duration. Roentgenographic examination revealed an infiltrative process along the right cardiac border (Figure 1). On August 5, examination of a specimen of sputum revealed cells which suggested the presence of malignancy (Figure 2). At bronchoscopy a polypoid tumor was found which seemed to originate from the posterior wall of the right main stem bronchus, 1 cm. below the carina. Results of study of a

biopsy specimen were negative but bronchial smears revealed malignant cells. Biopsy was repeated and the tissue revealed epidermoid carcinoma (Figure 3).

Case 2.—A 65-year-old white man was hospitalized on December 30, 1946. He had had hemoptysis, cough, had been raising mucus for two months and had lost weight during that time. The sputum was found to contain tubercle bacilli. On roentgenologic examination evidence of chronic bilateral inflammatory disease and a circumscribed density in the right upper lung field (Figure 4) were observed. Bronchoscopy on January 7 did not reveal abnormal findings. A

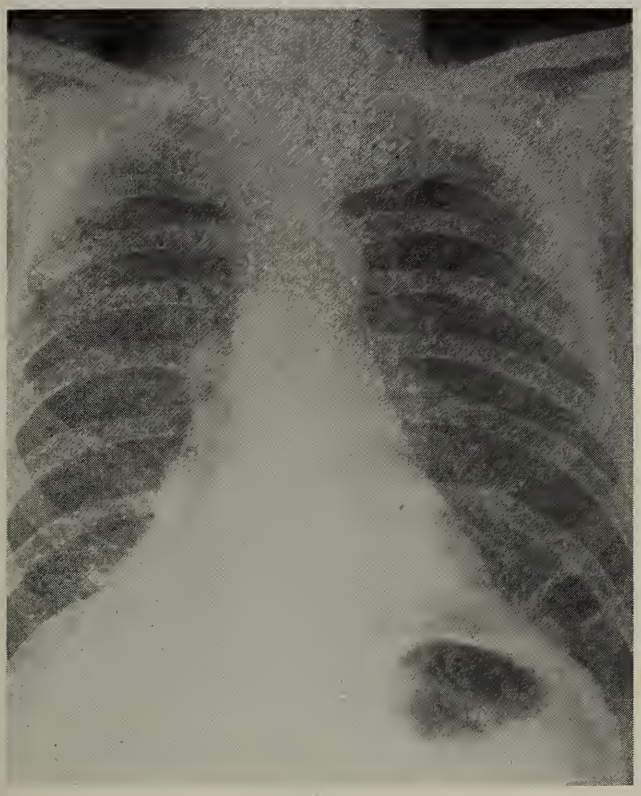


Figure 1

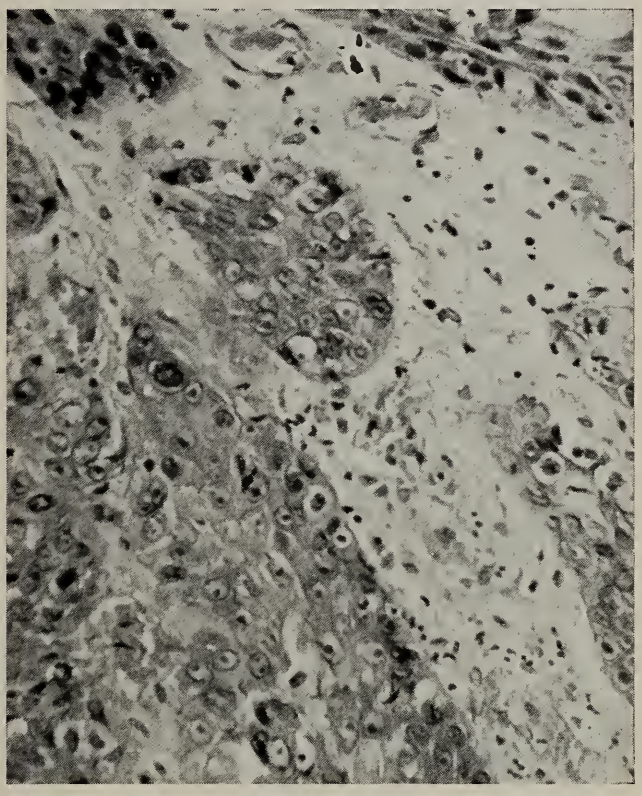


Figure 3

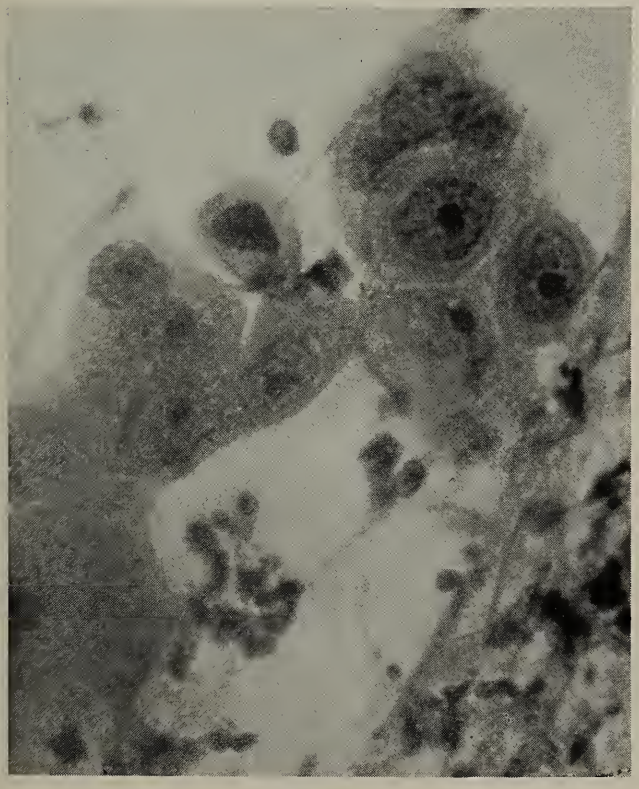


Figure 2

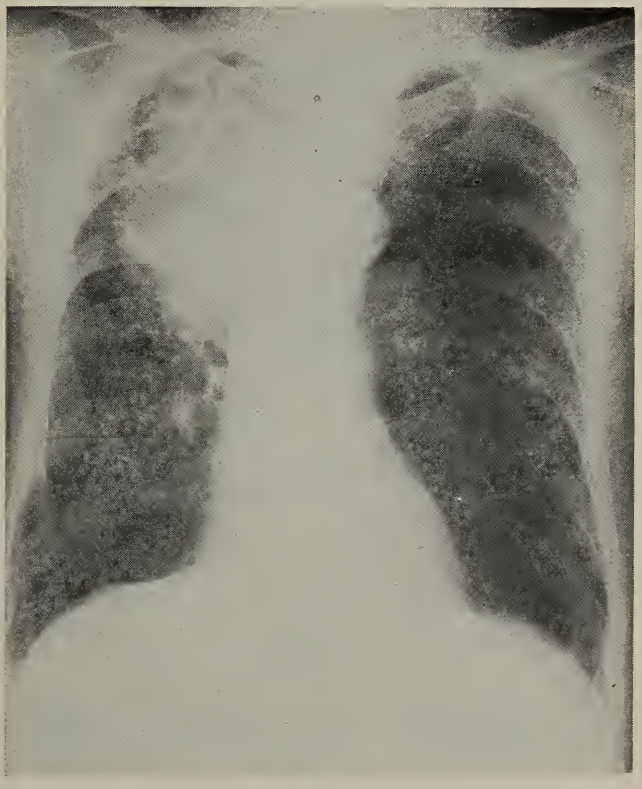


Figure 4

bronchogram revealed the presence of an obstructive lesion of the right upper lobe bronchus. In July sputum was submitted for cytologic study and was found to contain many malignant cells (Figure 5). The patient subsequently died and at autopsy an adenocarcinoma and coexistent pulmonary tuberculosis were found (Figure 6).



Figure 5

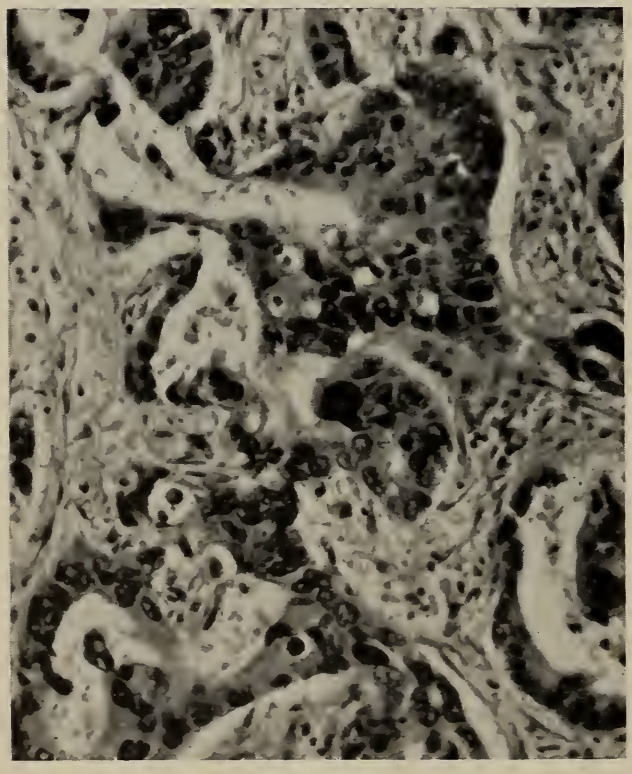


Figure 6

Case 3.—A 61-year-old white male was first seen by one of the authors in May, 1947. He had had pleuritic pain, cough productive of a small amount of blood on several occasions and night sweats for eight months, and he had lost weight. A roentgenogram revealed evidence of atelectasis of the lingular segment of the left upper lobe (Figure 7). On May 20, examination of a sputum specimen revealed malignant cells (Figure 8). A week later bronchoscopy revealed a mass in the left upper lobe and a rigid, deformed left main stem bronchus. Left pneumonectomy was per-



Figure 7

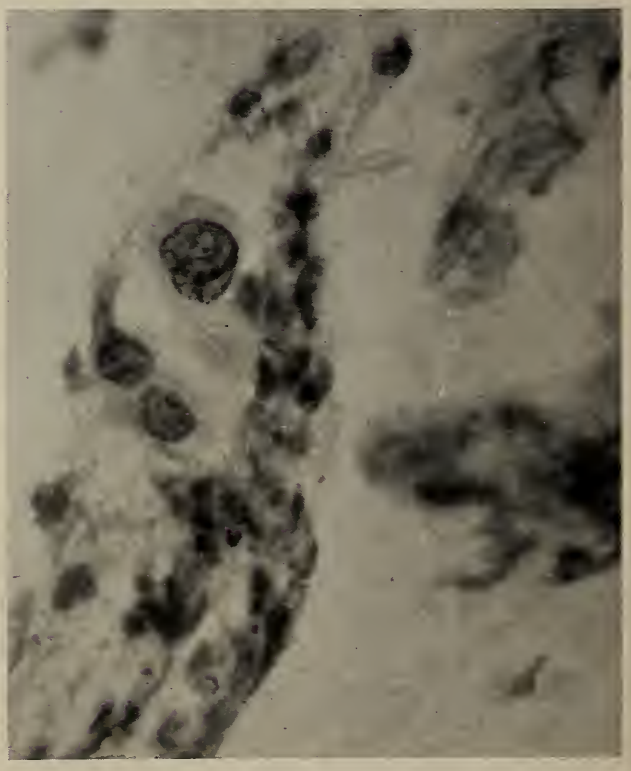


Figure 8

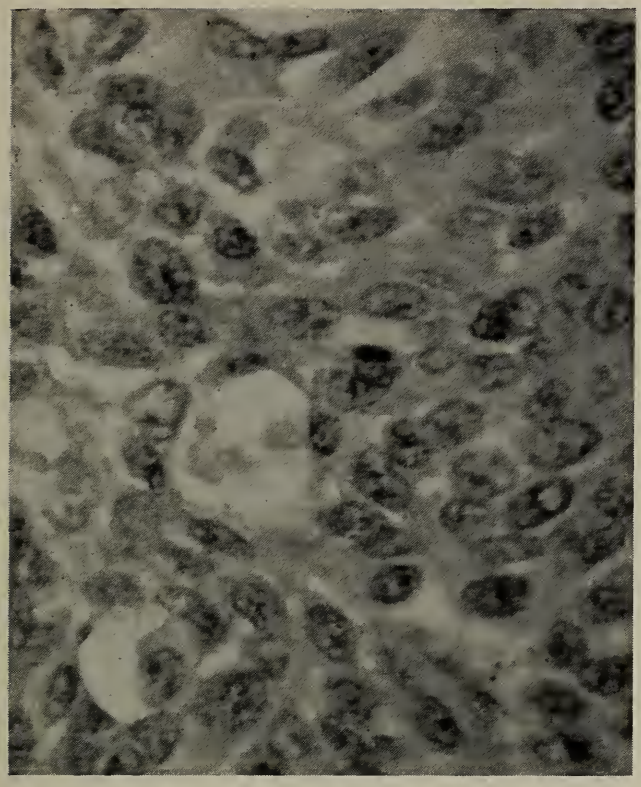


Figure 9

formed. Examination of the tissue revealed that a primary epidermoid carcinoma of the lung (Figure 9) was present.

COMMENT

The detection of malignant cells in the sputum is a relatively simple procedure. Malignant cells can be demonstrated in the sputum or bronchial secretions in at least 80 per cent of all patients with primary carcinoma of the lung. This figure compares most favorably with the results obtained by bronchoscopy with biopsy; it is considerably higher than the figures reported in many series of cases in which bronchoscopy and biopsy are used.[6] Skilled bronchoscopists are available only in certain medical centers. On the other hand, sputum can be prepared for study in any city or town and submitted to experienced observers. Bronchoscopy must be carried out, however, to evaluate the location and operability of the tumor.

Most bronchogenic carcinoma arise in the major bronchi and a considerable period may elapse before they reveal themselves on the roentgenogram by producing stenosis or a recognizable mass. During that time the tumor may metastasize. It may be possible to demonstrate exfoliated malignant cells in the sputum before roentgenologic changes appear. When the tumor develops in the peripheral portion of the lung it may produce roentgenographic changes early but the nature of these changes is difficult to evaluate. Prompt and thorough examination of the sputum, if indicated, and confirmation of the diagnosis of malignancy by cytologic study will lead to earlier and more frequent surgical treatment. This should enhance the chances for a favorable result from surgical resection.

If cancer is present, inability to demonstrate cancer cells in the sputum is frequently due to failure to examine a sufficient number of slides from an adequate *series* of specimens. It must be emphasized that failure to find malignant cells on smears made from a single specimen does not rule out the diagnosis of carcinoma any more than does a single negative result of examination of the sputum for tubercle bacilli exclude the possibility of tuberculosis. In our series whenever possible five or six slides made from each of five specimens were examined. At times it was found necessary to obtain more than five specimens before malignant cells were demonstrated.

SUMMARY

Exfoliated neoplastic cells in the sputum of patients with primary carcinoma of the lung can be identified in an appreciable percentage of cases after diligent examination. The utilization of the Papanicolaou technique for the examination of sputum and bronchial secretions is outlined. Three cases in which this procedure was of value in suggesting, establishing or confirming the diagnosis of bronchogenic carcinoma are reported.

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Practical Principles of Psychotherapy for the Non-Psychiatrically Trained Physician

Eugene Ziskind, M.D., *Los Angeles*

Introduction

This paper is motivated by the average physician's perplexity which arises when he is confronted with the "management" of patients who present neuroses or psychological problems. The experiences of the last war have focused attention on the importance of psychiatry to all branches of medicine, causing more interest on the part of physicians and greater receptivity on the part of the laity. The term psychosomatic medicine has given new dignity to the problems involved and more and more energies of the clinician are being devoted to the psyche in illnesses previously considered entirely physical or somatic. A large precentage (variously estimated at from 30 to 60 per cent) of patients seen in medical practice are affected with neuroses. There are not enough psychiatrists to meet this problem and it is not necessarily desirable that there should be. The specialist, however, should be of aid in delineating to the practitioner what procedures he can logically and most effectively utilize. All too frequently, because of conflicting schools of thought, the psychiatrist's advice has created confusion rather than clarity.

The recommended approach should be as largely devoid of the theoretical and controversial as possible, and the simple, common sense, and factual should be given first trial. The following recommendations are culled from experiences in outpatient department teaching of senior medical school students and the directing of a psychiatric clinic where volunteer psychiatrists of different disciplines (eclectics, psychobiologists, and psychoanalysts) treat ambulatory patients.

A word must be said as to the objectives of psychotherapy. As usually presented these are too formidable to be attained by the practitioner. Psychotherapy has become too much identified with the claims of classical psychoanalysis where therapy is intensive, prolonged and complicated by a hierarchy of theory—and correspondingly very expensive. This is frequently based on the erroneous premise that the individual, to get well, must undergo a complete character transformation or at least detailed and tedious exploration of past life experiences. Space does not permit a full discussion of all the principles involved. Suffice to say that fortunately the organism contains many forces operating toward maintaining good mental as well as physical health and all that is necessary in many instances is to give the organism a little boost over a difficulty so that the individual can effect the rest of the recovery himself. It is well to bear in mind that many psychogenic disorders are righted spontaneously without the aid of external intervention, at least without that based on recognizable scientific principles. Hence, in considering psychotherapy the following series of objectives arranged in order of increasing complexity may be entertained.

1. The establishment of insight that the symptoms are of psychogenic origin.
2. The removal of symptoms by relieving tensions in precipitating situational conflicts.
3. Attempts to resolve long-standing neurotic patterns.
4. Uncovering and removal of repression of traumatic early experiences where these are present and significantly related to the causation of the neurosis.

These objectives pass from the simple to the complex and perhaps only the first two are within the realm of the general practitioner, although possibly (and exceptionally) even the third. Surely the first, namely the ability to develop insight in the patient as to the emotional factors of his illness, is a most important objective and is often not difficult to attain. The physician, if he does nothing more for his patient, will serve a very useful purpose in shunting him from his search for more and more examinations, laboratory procedures and even unnecessary operations to attempt to ascertain the truly significant emotional tensions involved. Often this type of orientation, plus a prescription of the mental hygiene procedures which follow, is all that may be necessary to handle the patient's problem and at the same time serve an infinitely great value in preventing more serious protracted neurosis.

The attempt to relieve tensions and acute conflicts must most logically follow the uncovering of problems in the patient's total life situation, and often this can best be effected after the personal history has been taken. The interview treatment of chronic neurotic patterns is probably too complicated for the non-psychiatrically trained physician and belongs in the sphere of the specialist.

Application of Mental Hygiene Regimen

The great majority of psychoneurotics do not live up to the recognized standards of simple mental hygiene in their every-day life. This is readily appreciated by the patient. Recommendations to correct the deficiencies are usually easy to follow and involve a minimum of theorizing. Correspondingly, results are soon apparent. There will be some individuals, however, whose deep-seated conflicts may make it impossible for them to carry out these recommendations.

No attempt is made to cover the whole area, but instead attention is here given to a number of items which the author has found to be of practical importance.

1. *Sleep.* Because of the prevalence of the symptom of insomnia in the face of emotional problems, this item is given prominence in our discussion. Emphasis is placed on insisting that the patient spend no more than eight hours in bed. Failure to secure adequate rest the first night in bed creates physiologic demand for sleep the following night. The success following the actual enforcement of this prescription is striking in view of its simplicity. Its merit in preference to the common practice of using hypnotic drugs needs no further comment.

2. *Morning Shower.* Because of the prevalence of inertia, fatigue and ill feeling in the first hours after awakening, the necessity of tonic stimulation to the nervous system is generally appreciated. A hot or warm shower followed by an abrupt transition to cool or cold temperatures in the final one or two minutes has proven very satisfactory. Patients frequently comment upon its favorable effect.

3. *Diet.* Owing to the elimination one foodstuff after another as a suspected cause of gastro-intestinal symptoms, many a neurotic patient is on a deficiency diet. A normal diet high in protein, minerals and vitamins is prescribed. This gives the physician an opportunity to explain the mechanism whereby emotional tensions interfere with normal gastro-intestinal processes, thereby relieving the patient from the stigma that his symptoms are imaginary. The explanation of the production of visceral symptoms via the autonomic nervous system resulting from psychological stresses lays the basis for further psychomatic discussions. Emphasis is also placed on such hygienic aspects as avoiding hurry and emotional tensions at meal times and the encouragement of eating in company.

4. *Play.* Play and social activity are two of the chief forms of rest to the tense nervous system and the proper application of both these activities will often give the patient at least temporary respite from his emotional problems. Sports out of doors are preferred. Tennis and golf are among the best because they preclude the possibility of preoccupation. Play without the play spirit, "perfectionist striving," is cautioned against. Other forms of play instead of sports may be necessary for those unable to engage in such active exertion. Here the physician must rely upon his common sense and the ability of the patient to adapt the principles to his own needs.

5. *Social Activity.* Stress is placed on the necessity of planning one's recreation. Patients frequently require education and encouragement in the process of socialization and in replacing or adding to obligatory social activity (e.g. relatives, business associates) and thus attaining a social life more satisfying to their own needs. A minimum of two sessions of play and two sessions of social activity per week is desirable frequency for the average well person. In the presence of symptoms and in the absence of a full time job, the patient would do well to have two such "rest periods" for the nervous system each day.

Obviously these items do not cover the entire field of mental hygiene. These are features which can be universally applied. In addition many individual problems calling for recommendation will be apparrent, as to work, strivings, etc. The recommendations are simple to comprehend, the patient's progress with them is easy to follow and may be the basis for discussion on successive interviews.

COMMON SENSE APPROACH TO LIFE MALADAPTATIONS

Basic in the application of modern psychiatric principles to therapy is the recognition that nervous tensions and symptoms are engendered from conflicts resulting from frustration and blocking of urges, desires, and ambitions. The next therapeutic approach of increasing complexity is therefore evaluation of the patient's adjustment to life's major situations. This calls for a life history of the patient referable to early family relationships, schooling, occupational history, sexual, marital and parental experiences, life ambitions, philosophies and religious attitudes. It is essential that every physician become familiar with this history-taking as a part of his medical armamentarium. Such a history form is presented in Chart 1.

Obviously if the patient spontaneously presents the major emotional problem then formal history-taking may be unnecessary. There are even some who believe that history-taking interferes with the patient's recital of crucial feeling-laden material and misdirects the individual from assuming an active participation in the solution of his problem, placing it in the lap of the doctor. It has been our experience, however, in short-term therapy, that the omissions in the absence of such a history, have often been serious and that one can learn to handle the situation without the shortcomings mentioned.

From a record of the contributing and interfering factors in the major life adjustments, the physician is in a position to utilize logic as well as specialized knowledge in the discussion of these problems with his patient. This does not mean that the physician need take an active role in deciding or settling issues for the patient. More frequently a passive, non-directive[1] attitude permits the patient's feelings to come to the surface, with emotional releases which are more important in getting relief of symptoms and a crystallization of his adjustment than a purely intellectual solution of the problem. Indeed, discussion and resolution of the conflict involved may give the patient complete relief, particularly in the so-called situational neuroses. A more formal knowledge of the principles of psychotherapy, however, may be needed if clinical improvement does not occur without its application.

OUTLINE OF PSYCHOTHERAPEUTIC PROCEDURE

An outline of psychotherapeutic procedures, including those of most intricate psychiatric practice, may have merit for the general practitioner since it

CHART I

PERSONAL HISTORY

Birth and Early Development:

Mother's health during pregnancy; term; order of birth; hours of labor; presentation; instrumental delivery; rupture of bag of waters; birth cyanosis; birth weight; excessive crying after birth or difficulty in feeding; jaundice neonatorum. Age of teething, walking, talking.

Neuropathic stigmata; "nervous child," thumb sucking, bed wetting, nail biting, sleep walking, nightmares, tantrums, special fears.

Family Relationships and Environment:

Happy childhood? Adequate play life? Obedient? Sensitivities, geniality of environment.

Parents: Nervous manifestations, state of health, occupation, degree of skill and efficiency, religious attitude, relation to patient and to other children, social attitude, education and cultural background.

Siblings: Age, relationship, ties, jealousies, rivalries and comparisons.

Educational Adjustment:

Extent (number of schools also); efficiency and attitude.
Adjustment to teachers, students and objectives.
Extramural activities.

Occupational Adjustment:

Positions; duration and remuneration in each; reason for change; satisfaction.

Sexual Adjustment:

Pre-adolescent: Awareness; state of knowledge; experiences; attitude.

Adolescent: Age at first date; interest in opposite sex; frequency of social intercourse; attitude toward kissing and petting; "crushes" (overt and silent); masturbation; sexual preoccupation; sexual intercourse (friends, prostitutes, frequency, efficiency).

Adult: Marital, pre- or extra-marital sex relations; sex techniques and practices, adequacy, orgasm, contraceptive practices; compatibilities in marriage, physical, financial, cultural, ethical, parental and recreational. Separations, divorces, conflicts. Parental experiences.

Ideals:

Ideals, religion, philosophies, objectives and frustrations, political and social attitudes.

Hobbies, Recreations and Daily Routine:

Hobbies.

Recreations; out of door sports, play (cards, etc.) dancing, social activity, concerts.

Personality Traits:

Serious-minded, worrisome, sensitive, cry easily, harbor a grudge, suspicious, jealous, curious, envious, superstitious, seclusive, day dream, introvert.

Sad or happy, cyclothymic, irritable temperament, mix well, many friends, life of party, tell jokes.

Meticulousness as to belongings, person and work, punctual, resent waiting, opinionated, rigid, prudish, stubborn, generous or selfish, hypochondriacal, honest, conscientious, resent criticism, take a joke, pedantic.

Summary:

In terms of adjustment to each of major life situations.

calls attention to principles under which he can apply measures which common sense dictates in the absence of specialized knowledge and expert technique. It may aid in calling attention to possibilities he would otherwise overlook.

1. *Rapport.* The first step in all psychotherapeutic procedure is the establishment of rapport, or confidence. A careful examination and a kindly, sympathetic attitude towards the patient's problem often contribute most in this direction. Its effect in all medical therapy is great, even when not consciously appreciated. In its absence, psychotherapy can be little utilized, if at all.

2. *Ventilation or catharsis.* The beneficial results of permitting the patient to tell his story in his own way is universally recognized. There is a lessening of one's anxieties by "talking out" one's problems. Frequently this is very apparent to the patient. He will say, "Doctor, you have not done anything for me yet, but I feel much better. Just talking to you has helped me a great deal." This principle is recognized as the basis of many non-medical procedures of psychotherapeutic value. The value of confessionals and the efforts of the Oxford movement are largely traceable to this source.

The patient should be permitted and encouraged to do most of the talking. All too frequently there is the tendency for the physician to talk too much so that the material discussed is influenced by the doctor's preconceived ideas. One must avoid moralizing. The patient often has sufficient difficulty in talking of intimate life problems, without needing to face the possibility of disapproval by the therapist. Ours is not to pass judgment. We are interested in symptoms, not in sin.[2] Hence one must be not only a sympathetic listener but also a skillful listener.

Frequently crystallization of an amorphous, apparently insoluble conflict is accomplished in this manner and light shed where previously there had been dark uncertainty and fear.

3. *Desensitization.* In regard to many life problems the patient has repressions with pent-up emotions. Situations of this type have been referred to as complexes. Ventilation or catharsis may have helped only a little. It may require numerous discussions from many different approaches before the repressed experiences are uncovered with concomitant release of these pent-up emotions so that they are brought to the surface and dissipated. At times a precipitious, overdiligent attack on problems of great sensitivity make progress difficult since the patient is in no position to tolerate so painful an experience. He must be slowly eased into it.

Not infrequently the complex or emotional stresses are not apparent on simple history-taking. The physician may see his patient a number of times before essential material comes to light. Sometimes the information is willfully withheld or the patient may be unaware of the full significance of the material not divulged. A tendency for the patient to be embarrassed about, or to prefer not to discuss certain situations, or to belittle their significance, must be noted

as indicative of subjects to be cautiously but definitely discussed again. It is important to be on the lookout for underlying feeling, e.g. anxieties, guilt feelings, insecurities and aggressive reactions, instead of concentrating too fully on the intellectual content of the patient's story, since these frequently lead to the crux of the situation.

Because motivations in behavior are not always or even usually apparent, attempts to elicit material that the patient is not consciously aware of as being significant, are essential. It is in regard to the uncovering of these unconscious motivations, which is necessary for desensitization, that the many separate schools of psychiatry differ.

Special procedures for bringing such buried emotionally burdened conflicts to the surface include association tests, sodium amytal and pentothal interviews, hypnosis, the free association method of psycho-analysis and interpretations of dreams. Obviously, these more specialized uncovering techniques involve the most controversial and theoretical aspects of psychiatry and are for the specialist.

4. *Suggestion.* Suggestion, which includes assurance, encouragement, and persuasion, are psychotherapeutic procedures, frequently employed by all physicians. The role of prescriptions, placebos, physiotherapy, "bedside manner," and injections (some of which are often of questionable justification, in and of themselves) as suggestive measures is well recognized. The most intensive form of suggestion is hypnosis. Its use should be reserved for special situations by the specialist.

5. *Education.* Although a "non-directive" attitude in psychotherapy is considered most favored in most techniques, yet there is no psychotherapy in which the physician's thinking and attitudes does not play a role in influencing the patient. Obviously the degree to which this takes place in different techniques varies. It is doubtful whether one ever gets to the bottom of all one's personal difficulties in psychotherapy. It is important to recognize that in each individual there are resources operating toward wholesome growth and normality. In many instances, as stated previously, all the patient needs is to be given a boost over a particularly difficult situation and his natural resources do the rest of the job.

Discussion of inadequate adjustment to life situations, as revealed by the life history of the patient, leads to enlightenment in regard to life values, modes of living and overcoming insecurities, inadequacies and other maladaptations. Under the heading of education may also be listed those recommendations previously listed under "mental hygiene regimen." A common-sense appraisal of pertinent life situations involved is often invaluable. The physician may often be called upon for factual knowledge, particularly as to sexual matters. The development of insight, which is contributed to by many of the psychotherapeutic principles discussed, is also a matter of education and in this respect the understanding of the psychogenic origin of the illness is of paramount importance.

6. *Rehabilitation.* What can be done for the psychoneurotic patient in attempting to place him back in the ranks of the happy and efficiently adjusted individuals? First and foremost, the patient needs an adequate understanding and sympathy of his illness on the part of his family and friends. This interpretation should be the role of the attending physician. Help in the choice of occupation, securing special training, obtaining a position, and material aid for the patient and members of his family, and many other services which are available through community agencies and friends may be necessary in the rehabilitation.

When the physician has utilized these procedures, exhausting his fund of knowledge and common-sense approach to the apparent problems, and the patient is still in need of help, then the case becomes one for the psychiatrist. The program outlined, therefore, has merit not only in pointing out what direction the efforts of physicians who are not informed in the theory of psychiatric practice can best take, but also in setting up the indications for the specialist's care —indications not based solely on the ability of the patient to pay, as is so frequently the case.

The recommended procedures call for the application of principles from the simple to the complex. First there is the attempt to get the patient to live according to the best tenets of mental hygiene, a procedure designed to restore or develop a reserve of nervous stability. Then the physician approaches the life history of his patient to ascertain the adequacy of his adjustment to life's major situations and applies the principles of psychotherapy as his insight and untutored common sense dictate to him. Failing then, he looks for more expert aid.

It is to be lamented that the specialist so frequently, in his zeal and confidence in controversial techniques, neglects to obtain the benefits to be derived from the simpler measures. It is hoped that the recommendations made offer a practical outline for the non-specialist's approach to the psychoneuroses and psychosomatic problems of every-day medicine.

2007 Wilshire Boulevard.

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Pancreatic Lithiasis and Calcification

A Study of 22 Cases in a Series of 35,000 Necropsies

Weldon K. Bullock, M.D., and Hugh A. Edmondson, M.D., *Los Angeles*

THE presence of calculi within the ducts of the pancreas presents problems in pathogenesis, diagnosis and treatment which are difficult to solve. During the past decade, however, much progress has been made toward that end. In this paper we shall briefly review the problem and some of the more recent contributions to our knowledge, as well as report 22 additional instances of lithiasis or diffuse calcification of the pancreas.

As pancreatic calculi arise from the juice within the ducts, the normal chemical and physiological mechanisms involved in its elaboration are of basic importance. Pancreatic juice is secreted chiefly following meals, but continuous secretion in the fasting state in man is indicated by the experiments of Agren and Lagerlof[1] and Frisk and Welin[12] to be about 12 cc. per 20 minutes. Difficulties in arriving at the true figures include the exclusion of hydrochloric acid from the duodenum and the possibility of bile entering the duodenum and stimulating pancreatic secretion during this experiment. The total 24 hour secretion of the pancreas in man may be much higher than the usually accepted figure of 700 cc., according to Miller and Wiper.[21] They studied three patients with external pancreatic fistulae. One of these produced as much as 1,770 cc. in one day. As his digestion was not disturbed and the stools were normal as to fat content, sufficient amounts of juice were probably entering the duodenum for intestinal digestion. These authors, therefore, believed the total daily secretion in man might reach 2,400 cc. Harms[16] found the pressure within the ducts of the pancreas during the height of secretion to be considerably higher than that in the common bile duct; only during fasting was it lower.

The quality of the pancreatic juice differs greatly, depending upon the stimulating agent. With vagal or pilocarpine stimulation the juice is small in quantity and high in enzyme activity. With secretin stimulation the juice is much greater in quantity, more alkaline and poor in enzymes. Komarov, Langstroth and McRae[18] in 1939 confirmed and further elaborated the work of Ball[4] in 1930 and that of Gamble and McIver[13] in 1928 regarding, first, the relationship of chloride and bicarbonate fractions to the degree of alkalinity and, secondly, the similarity of the inorganic constituents of the juice to the level of the same ions in the blood serum. In the juice of both dogs and man the inorganic ions are chiefly sodium, bicarbonate and chloride. The other ions—potassium, calcium, magnesium and phosphate—are present in much smaller quantities. Injection of sodium and potassium into the blood stream increases their content in the blood serum and pancreatic juice to the same degree. Thus it is assumed that the pancreatic acini are freely permeable to these ions. Calcium, magnesium and phosphate are secreted with much more difficulty. Ball also demonstrated in dogs that the blood serum and pancreatic juice had identical osmotic pressures. The pH of the juice increases with secretory activity. This is due to an increase in the bicarbonate fraction and a concomitant decrease in the chloride. However, the sum of the two remains constant. Ball observed during the height of secretory activity a pH of 8.24. He calculated that 8.3 was the maximum pH the pancreatic juice could reach by assuming a free CO_2 concentration of 1 millimol and a maximum bicarbonate of 150 millimols.

Most pancreatic calculi are composed chiefly of calcium carbonate and small quanities of tribasic calcium phosphate. Magnesium carbonate and calcium oxalate have occasionally been observed. Stones have also been classified into inorganic and organic types, the latter containing fat, fatty acids, carbon, cholesterol and albumin, bound together with calcium salts.[7] It has been assumed by many that because of the low concentration (1 to 1.7 millimols) of calcium in the pancreatic juice the formation of calcium carbonate calculi is difficult to explain and that additional factors such as inflammation with outpouring of more calcium might be necessary. On theoretical grounds this may be disputed if one takes into consideration the fact that the pH in the human pancreatic juice goes as high as 8 and the bicarbonate as high as 127 millimols.[3] Under these conditions the solution, even with 1 millimol of calcium present, is supersaturated.*

Pancreatic lithiasis may be symptomless or there may be a long history of upper abdominal complaints. The occurrence of solitary stones without symptoms is not unusual and their origin is only conjectural. Comfort, Gambill and Baggenstoss[10] at the Mayo Clinic in 1946 made an outstanding contribution in their study of 29 cases of primary "chronic relapsing pancreatitis." The disease is characterized by repeated attacks of upper abdominal pain, elevated serum amylase and lipase values and often temporary derangement of both the external and islet cell secretions. With repeated attacks the latter changes may become permanent and diabetes mellitus, steatorrhea and creatorrhea may be present. Stones or diffuse calcification was diagnosed in 14 of the 29 cases. Comfort and his co-workers divided these 29 patients into seven clinicopathological

From the Department of Pathology, School of Medicine of the University of Southern California, and the Laboratory of the Los Angeles County Hospital.

*Detailed calculations regarding the physical chemistry involved will be published in the future in collaboration with John W. Mehl, Ph.D.

groups, depending upon the presence of pain alone or various combinations of pain followed by one or more of the major complications: diabetes mellitus, steatorrhea or lithiasis. They believed the stones were secondary to the pancreatitis and observed the formation of calculi, while patients were under their care, within one to fourteeen years after the onset of pancreatitis. This disease is of great importance because a diagnosis can so often be made with great certainty. The exact mechanism of stone formation in the ducts of a pancreas subject to repeated attacks of inflammation is not known. Obstruction, stasis, epithelial desquamation and inflammatory exudate may all play a part in instigating the process. Alcohol probably acts only in precipitating the pancreatitis by overstimulation. Jaleski[17] noted that 45 per cent of the patients having pancreatic lithiasis reported in the literature were alcoholics. Recently Wechsler and Weimer[26] reported two younger individuals with pancreatic lithiasis whose abdominal symptoms began in childhood at the ages of eight and ten, and the calculi were diagnosed at the ages of 27 and 28. These patients were not alcoholics. It has been suggested that there is a possibility of calculi being a late complication of cystic fibrosis of the pancreas, a disease usually seen in the first two years of life.

The incidence of pancreatic lithiasis is low. In nearly all articles on the subject the total number reported in the literature is mentioned and brought up to date. The latest tabulation noted is that of Lionello, Ficarra and Ryan,[19] in which the total reported was 225. As the total number appears to be growing at a more rapid rate, its importance seems to be diminishing. The incidence in various autopsy series varies considerably. Pascucci[22] tabulated all those reported previous to 1944. There were 52 instances in a total of 117,031 routine necropsies, an incidence of 0.044 per cent.

Beling[5] in 1940 first made the suggestion that diffuse calcification of the pancreas be separated from the more common form of the disease in which there are only discrete intraductal calculi. He collected 12 instances from the literature and added one. He gives Allen[2] credit for the first reported case in 1903. Wirts and Snape[27] in 1947 collected 22 cases from the literature plus two of their own. The patients have minute calculi in the finer ducts and in the acini. The calcification is said not to involve the epithelium of the acini. Severe interlobular fibrosis and acinar atrophy are usually present. The larger ducts may be dilated and also contain minute calculi. The basis for separation of this group is that apparently the disease begins in the smaller ducts or acini and involves the entire gland, producing a stone-hard organ that can be distinguished by x-ray examination to have a separate pattern. From the clinical standpoint this group is closely similar to the larger one in which sizable calculi are in the ducts.

DIAGNOSIS

Many articles have dealt with the diagnosis of pancreatic calculi. It is agreed that a flat roentgenogram of the pancreatic area is of most importance. This should be made before any barium is present in the digestive tract or gallbladder dye studies are attempted. If shadows are present in the pancreatic area, Beling[6] emphasizes the importance of lateral films in order to bring out their relationship to the spine. The pancreas lies 1 or 2 cm. in front of the spine, although the tail may be curved and on the same plane as the body of the vertebrae. Four types of calculi have been described by Gillies.[14] The differentiation of disseminated calcification from discrete calculi depends upon the demonstration of a diffuse, stippled calcification involving the head, body and tail.[27] In addition to roentgenologic evidence of calcification in the pancreas, studies of the external secretions are of importance. A notable step in this direction was made by Agren and Lagerlof.[1] They have introduced the use of a specially designed double-lumened tube, to be introduced into the stomach and duodenum, which aspirates both gastric and duodenal secretions at the same time. With secretin injection intravenously there is a prompt increase in the volume of the pancreatic juice and especially an increase in bicarbonate and enzymes. In both chronic pancreatitis and stone, marked reduction in volume, alkalinity and enzymes may be observed.[9] In recurrent attacks of pain associated with chronic pancreatic disease with or without calculi, studies of serum amylase and lipase[10] are most helpful. It is to be remembered that in long-standing obstruction by stone in the head of the pancreas coincidental with acinar atrophy the levels of amylase and lipase tend to decrease in recurrent attacks of pancreatitis. Other laboratory aids to diagnosis are well known and no particularly new developments have been noted. These include examination of the stools for fat and the percentages of neutral fat and fatty acids, tests for glycosuria and glucose tolerance tests.

REPORT OF CASES

There were 22 instances of pancreatic lithiasis and/or calcification among 35,000 consecutive autopsies performed between September 15, 1925, and August 19, 1947. They were evenly divided as to sex. The range of age was from 22 to 86 years, the mean age for the entire group being 53.4 years. The males were considerably older, the mean being 64.1 as against 43.6 for the females. Death was attributable directly to chronic pancreatitis and lithiasis in seven cases, and the disease was contributory in six. In the remaining nine instances the pancreatic disease was not a direct factor in the cause of death.

Clinical:

The symptoms and signs of the disease were not definitive. The following were noted at the time of the admission of the patients to the hospital.

Symptoms		Signs	
Upper abdominal pain	10	Weight loss	17
Weakness	8	Hepatic enlargement	11
Nausea and vomiting	8	Jaundice	5*
Constipation	6	Edema	1
Diabetes (thirst, polyuria or coma)	6	Ascites	1
Steatorrhea	1		

*In addition the examining doctors later noted icterus in nine additional cases, making a total of 14.

The chief presenting symptom was upper abdominal pain of some kind. No two patients complained of exactly the same symptoms. In some the pain was of a severe colicky nature, while in others it was a vague distress. Radiation of the pain was likewise of little assistance in making a diagnosis. Sometimes it would radiate to the right upper quadrant, other times through to the mid-portion of the back. The pain seldom resembled that of biliary colic. One of the patients had pain in both flanks and was thought to have an acute pyelonephritis. The pain of pancreatic lithiasis is often associated with nausea and vomiting, but the two do not necessarily go together.

The other symptoms and signs noted by the patients, such as weakness, loss of weight and constipation, are of no help in arriving at a correct diagnosis. Steatorrhea occurred but once in this series; other forms of diarrhea were absent. Diabetes mellitus occurred in seven instances, and in six instances it was the primary reason for the patient's entry to the hospital. In one patient the disease was latent, being diagnosed by the glucose tolerance test. Four patients did not complain of pain. One was known to have had diabetes for three years, which had been controlled by diet until two days previous to final entry into the hospital. Jaundice was an outstanding sign in 14 instances, although only five patients noticed the icterus. The diagnosis of chronic pancreatitis with lithiasis was not made clinically in any of the 22 cases. A specimen taken of the head of the pancreas in one patient operated upon for obstructive jaundice resulted in a report of chronic interstitial pancreatitis. At necropsy this was confirmed but the underlying cause was intraductal calculi.

There was a definite history of long use of alcohol in ten instances. In two the matter was questionable, and in ten cases there was no notation of intake of alcohol.

The histories of two of the patients are of particular interest. One of these had obstructive jaundic due to pressure on the common duct and the case was reported in detail at the Clinical-Pathological Conference of the California Medical Association on May 3, 1947, by Dr. John Tragerman (published in California Medicine, 67:256-258, October, 1947). The second case is as follows:

CASE REPORT

A white male mechanic, age 45, first came to the outpatient department on May 3, 1934, complaining of "bloating of the abdomen," a condition that had existed for 18 years. This would often cause so much distress that nausea and vomiting would result, with subsequent relief. No true abdominal pain was associated. Soda gave no relief. The attacks would last from one to five days and would recur every six to twelve months. For one year the patient's appetite had been poor and he had lost 15 pounds in weight. He used alcohol, but the history does not state in what quantities. On May 9 barium study revealed an irregular, tender duodenal cap. A diagnosis of duodenal ulcer was made. The patient returned to the outpatient department in June and July of 1934 complaining only of severe upper abdominal pain. He entered the hospital on August 13, 1935, complaining of similar pain but refused treatment and was discharged. He reentered the hospital September 2, 1935, from another hospital in a moribund condition and died a few hours later. At necropsy no evidence of a duodenal ulcer was identified. The cause of death was a solitary stone in the duct of Wirsung with a complicating acute pancreatitis.

This history illustrates the difficulty in differential diagnosis between pancreatic calculi and duodenal ulcer.

Pathology:

Study of specimens in this series revealed only the end stages of obstructive disease of the pancreatic duct and therefore tells us very little of the genesis of the calculi.

Gross Pathology: The descriptions of the pancreases in gross are of interest chiefly from the standpoint of the location of the calculi and their complications. In nine cases calculi were within 2.5 cm. of the ampulla Vater. In two of these cases the calculi had obstructed the common duct, apparently by pressure and edema, which resulted in jaundice in both patients and biliary cirrhosis in one. Of particular interest was a large ivory-like stone which obstructed the duct of Wirsung in the head of the pancreas, but there was little dilatation or change in the duct system behind the obstruction. This brings up a point which apears to have been omitted in most published discussions of pancreatic calculi; that is, whether or not the communicating duct of Santorini may carry the pancreatic secretions to the duodenum when the duct of Wirsung is blocked. In ten patients the calculi were in the body or tail, or were described as being widespread in the duct system but no definite location was given. There were three instances of diffuse calcification of the pancreas, so-called petrificans, without stones in the duct. Of the entire group of patients, 16 had multiple calculi or calcification, and in six there was a solitary stone within the duct. Seven had one or more cysts somewhere in the pancreas. Some of these were apparently dilatations of ducts and others were pseudocysts. The complications were what one would expect with obstruction of the duct: three had acute pancreatic necrosis; two, healing fat necrosis; in four there was evidence of purulent inflammation, with solitary abscesses having resulted in two of them.

Microscopic Pathology: The microscopic changes were of interest because of the variations in degree of dilatation of the duct and fibrosis of the pancreas. With apparently similar degrees of gross obstruction there was great variation in microscopic evidence of dilatation. This again emphasizes the possibility of some of the pancreatic juice escaping through the duct of Santorini. Regardless of the degree of dilatation of the duct, dilatation of the acini was minimal or even absent. Rich[24] has proven that with increased pressure within the ducts fluid easily escapes between the acinar cells into the peripancreatic tissue. Diffuse perilobular and intralobular fibrosis were common, but atrophy alone appeared to have occurred in some instances, leaving little evidence of chronic inflammation and fibrosis. In some of those patients with solitary calculi, dilatation and atrophy alone were observed. The question of what role

repeated attacks of pancreatitis have in the formation of fibrous tissue arises but cannot be solved from this material. Islets apparently are not always, as has been taught, spared until the last. One of the patients had diabetes mellitus without great acinar atrophy or evidence of steatorrhea.

Associated Pathology: There were 14 in whom the liver was fatty. Eleven of these had cirrhosis. In eight it was Laennec's type; in two it was biliary cirrhosis due to obstruction of the common duct by a stone in the duct of Wirsung; and in one the cirrhosis was of the fatty dietary type with no particular relationship to periportal spaces or central veins—a condition similar to that described by Chaikoff[8] in experimental dietary fatty cirrhosis of animals.

COMMENT

It seems strange that in such a large series as this not a single correct diagnosis was made antemortem in spite of the fact that many of the known symptoms of pancreatic calculi were present. Because pancreatic disease was not suspected, laboratory procedures useful in diagnosis were not performed. One patient had a roentgengram of the pancreatic area which showed calcification but this was interpreted as an artifact. The incidence of the disease in this necropsy series, 0.062 per cent, is somewhat higher than the general average of 0.044 per cent reported by Pascucci.[22] Six of the 22 patients in our series were seen within the year preceding the preparation of this paper. All were chronic alcoholics. During the same period calculi was diagnosed in a patient on the wards and we were consulted about another case by one of our colleagues. Thus, having seen or known of eight instances of the disease in one year, we feel that it hardly belongs among the rare diseases. Taking into consideration the present consumption of alcohol and the number of chronic alcoholics in the population, an increase in incidence of pancreatic lithiasis might be expected. The incidence in this series is probably much too low, as often the pancreatic ducts were not dissected at autopsy. At present we are examining a series by postmortem roentgenograms to compare with Ludin's[20] series in Basel. Ludin carefully dissected all pancreases showing calcific roentgenographic shadows and found 28 stones in 542 pancreases, giving an incidence of 5.1 per cent.

The complications of lithiasis in this series are similar to those that have been reported. Among the local disturbances within the pancreas are atrophy, acute pancreatitis, abscesses and pseudocysts. Many of the stones were probably due to recurrent attacks of pancreatitis of the type described by Comfort.[10] In patients with symptomless solitary stones in whom no evidence of chronic inflammation was noted, other explanations for the formation of calculi should be considered. In four of the six patients with solitary calculi no symptoms attributable to the pancreas were elicited. It is possible, of course, that a minimal attack of pancreatitis forgotten by the patient could give rise to a stone.

Complications arising from pressure on contiguous structures, especially the common duct and duodenum, should be remembered. Additional pressure phenomena mentioned by Comfort[10] include pressure on the splenic vein and mesenteric vessels.

Perhaps the pathological physiological sequelae are the most interesting of all. These include diabetes mellitus, steatorrhea and fatty metamorphosis of the liver with or without cirrhosis. Increase in serum amylase and lipase may occur in the recurrent attacks of pancreatitis which often characterize the disease. Any of these, when present, constitute important leads to correct diagnosis. Flat films of the pancreatic region are now being requested on all patients entering the hospital in an acute attack of pancreatitis. It may be questionable from the economic standpoint whether the same procedure should be done on all diabetic persons. Seven, or 31.8 per cent, of the 22 patients in this series were diabetics. From the histological study of these it appears that occasionally the atrophy of the islets and acini proceeds at a parallel rate and the islets are not preserved until the last. In Comfort's[10] series of 29 there were four patients who had upper abdominal pain followed by diabetes and calcification, but there was no evidence of steatorrhea. Two causes for this may be mentioned: First, the calculi or calcification may involve primarily the body and tail, where most of the islets are present; even though there were great destruction here, the acinar tissue in the head of the pancreas might produce sufficient external secretion to prevent steatorrhea. Second, once islet tissue is partially destroyed, episodes of hyperglycemia may produce progressive damage to the islets alone, the effect being somewhat similar to that seen in experimental animals, both normal and partially depancreatized, in which prolonged intraperitoneal glucose-saline solution with hyperglycemia produced permanent damage to the islets.[11] The low incidence of steatorrhea (one in twenty-two) probably means that the stools were not examined carefully. The fatty change noted in the liver with or without cirrhosis was in every instance associated with chronic alcoholism.

The treatment of pancreatic lithiasis, when possible, is surgical.[15, 25] Discussion of this subject is beyond the scope of this paper. Haggard and Kirtley state that the results are good following the removal of stones. Early diagnosis and surgical treatment are emphasized by most authors. The importance of control of pain by sympathectomy and vagotomy has recently been introduced by Reinhoff and Baker.[23]

SUMMARY

1. Twenty-two instances of pancreatic calculi and/or calcification in a series of 35,000 necropsies are reported.

2. In 14 of these there were multiple calculi; in five they were solitary. Stones lodge most commonly in the first 3 cm. of the duct of Wirsung.

3. Calcinosis or diffuse calcification were present in four cases, and in three of these four there were no grossly detectable intraductal calculi.

4. Dilatation of the ducts, atrophy of the parenchyma, fibrosis and chronic inflammation occurred to a varying degree.

5. Fatal complications included acute pancreatitis, suppuration of the pancreas, and obstruction of the common bile duct.

6. Atrophy of acini and of islets may occasionally proceed at a more parallel rate than is usually recognized. Diabetes mellitus was present in seven patients in this series.

7. The signs and symptoms of the disease in this series were difficult of evaluation. Not a single case was diagnosed correctly.

8. The most important diagnostic aid is roentgenograms of the pancreas.

9. Alcoholism and recurrent pancreatitis resulting in fibrosis are common precursors of calculi and calcification. Ten in this series were chronic alcoholics.

10. Pain, weight loss, jaundice, and a palpable liver were the predominating clinical manifestations.

11. The disease may be symptomless.

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A Pediatrician's Observations on Mental Hygiene

Victor E. Stork, M.D., *Los Angeles*

IT would be both inappropriate and presumptuous for a pediatrician to attempt to inform an audience composed largely of psychiatrists on the general principles of mental hygiene as applied to children. It is, in fact, the psychiatrists who have provided much of the material on which our interest is based. The writer will simply try to present briefly what he thinks the present attitude of pediatricians on this subject is, and something of the why and how this attitude has been reached.

Many of us began our pediatric practice in happy ignorance of such things as conflicts and neuroses and long before the term "mental hygiene" was coined. Behavior, attitudes, and parent-child relationships had no more to do with clinical pediatrics than had astronomy. We thought we knew something of growth and development and physiology and pathology on the physical side and how to diagnose and treat the various physical defects, abnormalities, infections, and accidents. But it was indeed a shock to discover very quickly that pediatrics is not like that. When we took our first history, asked for the chief complaint, and were told, "This child, since the arrival of his little sister several weeks ago, has become sullen, disobedient, and destructive," then we realized that there had been gaps in our education. We suspected jealousy was the cause of the child's behavior, but had no idea what to do about it. We made feeble attempts to solve some of these problems, using a bizarre mixture of common sense, intuition, general experience, a few shreds of popular psychology, and a few guesses thrown in. Some of us developed an amazing aptitude for giving parents the wrong answers. Others adroitly evaded these questions, claiming a steadfast interest in strict clinical medicine, and looking hopefully for a case of pancreatic fibrosis or glycogen storage disease, meanwhile telling the mother of the child who wouldn't eat to "make him finish his plate and insist on the correct balance and the optimum number of calories."

But as time went on, and with the advancement of knowledge, the whole concept of the function and scope of pediatrics broadened. We became interested in the total welfare of the child and found ourselves, as Gesel says, "holding the most strategic position in the whole scheme of preventive and constructive medicine, since health protection begins with the beginning of life and growth." And we learned to think of the child as an indivisible unit in which physical well-being and mental welfare are reciprocal and inseparable. Then we began to see that our responsibility as pediatricians had expanded and that now we must help develop not only the best organic mechanism but the most satisfactory personality of which the child is intrinsically capable.

We began our search for sound scientific knowledge in the field of mental health, absorbing new studies in growth and development, groping our way through the strange and unfamiliar vernacular of the psychiatrists, listening to conferences at the child guidance clinics, picking up a morsel here and a bit there and trying to reject the unscientific overpopularized material—that of the cults and the superficial forms of pseudo-psychologic doctrine which have crowded the radio and the popular magazines. In his search for knowledge the writer even enticed a first rate psychiatric social worker into his office and over a period of years watched her uncanny skill in ferreting out the causes of unsatisfactory behavior and in improving parent-child relationships.*

But at the risk of being accused of prejudice or of pride in profession, it must be recorded that we pediatricians are now learning more from each other than from any one else. That is to say, the studies and papers and books of pediatricians themselves are making the greatest contribution—perhaps because they are written from the pediatric point of view. The writings of such men as Aldrich and Spock provide the sort of sound and practical material with which one can build the tools and the method of his daily work.

We have practically abandoned the term "mental hygiene." Hygiene refers largely to the science of sanitation and one often thinks of it in connection with septics tanks, typhoid control, or such things as the prevention of dental caries. We prefer the term "mental health" and we think of a mentally healthy child as one who is growing in self-control and self-direction toward social ends—one who is developing an adequate personality, and one who is growing mentally and emotionally toward maturity. This growth takes place largely through his personal relationships and if his mental health is properly fostered he should, we think, eventually become a maselves in a typical pediatric office, not in terms of the well known symptoms demonstrated by the inture person, intellectually, emotionally, socially, and morally, which after all is what we are trying to accomplish.

We have learned that growing children thrive best

Read before a joint meeting of the Sections on Neuropsychiatry, Public Health and Pediatrics at the 76th Annual Session of the California Medical Association in Los Angeles, April 30-May 3, 1947.

*In contrast to these crude beginnings of the study of mental factors in child development, it is interesting to note the form these studies are taking now. Since this paper was written there has been held in Hershey, Pa., a most valuable conference on the mental health aspects of Pediatrics "for the exchange of information between two medical disciplines dealing with children—pediatrics and child psychiatry." It is both revealing and heartening to read the reports of this conference and to hear what is actually being done through the joint efforts of pediatricians, psychologists, and child psychiatrists in teaching, in practice, and in research at such medical centers as Cornell, Columbia, Minnesota, Harvard, Yale, Hopkins, Chicago, California, and Stanford.

mentally when they live in a climate of human attitudes and relationships which satisfies certain basic needs. And in order to prevent the stresses and strains which may lead to mental ill health we try to see that these basic needs are fulfilled. When we meet a problem in behavior (which we do almost every hour of every working day) we try to solve it in terms of unsatisfied needs.

In simplified form, the more important of these basic needs for the growing child we conceive to be as follows:

1. The need of security. We feel that the approval and affection which satisfy this need should be deserved, so that the child learns to acquire security through his own efforts.

2. The need to live in and face the actual reality of the world as it is and the people he has to live with, including himself. He must learn to control his impulses and fit them to social demands and he especially needs to develop the courage to face real facts and real situations without being hurt. He must stand up to life without evasion or retreat.

3. The need for activity leading to achievement which results in satisfaction. This includes the need for the recognition and friendship of contemporaries —the need for success.

4. The need for independence appropriate to age.

The pediatrician feels that when such basic needs as these are not met there is apt to be a problem expressed in terms of unhealthy attitudes and actions. The child is in distress emotionally and his conduct represents an effort to solve the problem. And when a child attempts to solve his own problem he often gets into difficulties with his behavior, which is poor mental health. And it is also true that as these needs *are* met the necessity of an imposed external discipline sinks into the background. When we can connect such symptoms as lying, truancy, enuresis, fears, temper tantrums, destructiveness, jealousy, or negativism with *insecurity*, for instance, we are already well on the road to treatment. Better still, by fostering security in the beginning, we are well on the road to prevention.

We think we have made considerable progress lately in fulfilling the need for independence appropriate to age. We have stopped regimenting infants into fixed schedules and rigid techniques. We have stopped "breaking" them into and out of habits at certain fixed and specific ages. We feel that the child has a right to pursue his own growth pattern, a right to be given food when he is hungry, and a right to refuse it if he isn't hungry. We are alert to help him take his next step ahead when he is ready to take it, but we respect his right to go along on his own individual developmental time-table.

It might be of interest to list a few of the most common problems in mental health which present themfant or child, but in terms of certain attitudes often indulged in by the parents. We see the fearful and anxious mother, overpowered by her sense of responsibility, constantly alarmed and in need of reassurance; the grimly determined and domineering mother who tries to force her child into habits, who creates issues and then imposes her authority in settling them, and who fights on down to the last bit of spinach; the over-protective and often possessive mother who tries to shield her child from all that may be unpleasant; the over-submissive mother who allows her child to make unreasonable demands and get them fulfilled; the frustrated mother who has read all the books but can't find the right answers for *her* child and has lost all spontaneity as well as her sense of humor; the nagging, scolding, threatening mother who expects adult behavior at the five-year level; the mother who wants to give her child what she herself lacked in her childhood; the mother who allows the grandmother to direct all operations because she herself has never become emancipated from maternal control; the mother who holds too tight a rein over her adolescent daughter; the mother who sees only the annoying faults but none of the assets of her child; and, to help balance the parental scale, the father who expects his child to jump through the hoop with perfect and prompt obedience when he snaps his fingers.

Our method of treating such destructive attitudes is through discussions of the principles involved and by giving didactic advice patiently and tactfully. The psychiatrist would doubtless consider this a crude method but there can be no doubt of its effectiveness so long as we stay clear of deeply rooted conflicts and well developed neuroses, so long as we stay fairly close to the surface, and so long as we keep clearly in mind our aim—to promote sound mental health. And for the sake of the record let it be said that there are many parents who, through the intelligent application of sound principles, do know and practice most of the rules of the game and whose children therefore do have excellent mental health.

But we do not expect our parents to create a letter perfect environment of human relations for their children. We tell them that the tree which is blown about a bit by the wind puts down stronger roots and that the child who must meet and solve a few irritations thereby builds stronger character.

Over and above all and in a much larger sense, as citizens as well as pediatricians, we see clearly that if we want a better world we shall have to inhabit it with better people. If we want to preserve and strengthen our civilization we shall have to improve the science and art and practice of human relations in the oncoming generations. We shall have to help our children grow into truly mature adults with wholesome minds and with moral strength. For sound psychology and sound ethics fit together and dove-tail at every point, and when these are further enhanced by a sound sense of spiritual values, we have done our utmost. If we can keep this ultimate aim sharply in focus the concept of mental health will constantly grow in power, in dignity, and in overriding importance.

1136 West Sixth Street.

Discussion by Carl A. Erickson, M.D., *Pasadena*

I enjoyed Dr. Stork's paper very much and I'm sure that everyone can see why he is considered a leader in his understanding of the psychologic side of pediatric practice.

I'd like to emphasize that it is the pediatrician's responsibility to turn out not only a physically healthy specimen but also a person with agreeable disposition and personality.

The origins of this personality stem back into early childhood and, in fact, into infancy. Perhaps cases of suddenly disturbed personality do occur but usually the cause is searched for in the person's earlier history and if we pursue this back all the way we reach infancy. So, as pediatricians we should try to help parents avoid some of the tensions and frictions that arise between them and the baby which might, if allowed to progress, lead to disturbed behavior later on. Matters such as schedules, feeding, weaning, training, and discipline are likely sources of trouble and it should be the pediatrician's duty to adequately discuss these matters ahead of time so that upsets will be avoided.

We pediatricians should have more training along this line if we are to do a good job because during these early critical years we are usually the only physician that is seeing the child, and it is our advice that is sought in the handling of many problems. We have the Child Guidance Clinics and I suppose that the pediatricians can be thought of as running infant guidance clinics as well as tending to the food and vitamin needs of our patients.

The Treatment of Cardiovascular Syphilis

Olov A. Blomquist, M.D., *Los Angeles*

A SURVEY of the modern treatment of cardiovascular syphilis demands consideration of three fundamental principles. First is that cardiovascular syphilis may be almost entirely prevented by the adequate treatment of early syphilis. The second is the avoidance of serious treatment reactions which may incapacitate the patient or cause his death. The third is that to be beneficial adequate doses of the arsenical drugs must be given.

PREVENTION OF CARDIOVASCULAR SYPHILIS

Adequate treatment early in the course of the syphilitic process offers almost complete protection against the development of cardiovascular syphilis. Consequently this complication would seldom, if ever, be seen if all syphilis could be diagnosed and treated early. Even when treatment is not given until the phase of late latency the degree of protection is very gratifying. Because in recent years many patients have been treated adequately and relatively early in the course of the infection, the incidence of new cases of cardiovascular syphilis is rapidly decreasing.

AVOIDING SERIOUS TREATMENT REACTIONS

Serious treatment reactions of the Herxheimer type (or therapeutic paradox) usually occur because the patient is given strongly spirochetocidal drugs before being adequately prepared for them. This is an age in which vigorous anti-syphilitic treatment is commonly used. Such treatment is desirable in all patients having early or uncomplicated syphilis. However, when evidence of organic disease due to syphilis exists and the disease appears to be of such nature that a Herxheimer reaction might be expected, we should proceed with mildly spirochetocidal drugs such as bismuth until danger of a Herxheimer reaction is past.

Cardiovascular syphilis is one of the manifestations of syphilis in which the Herxheimer reaction may be extremely serious or even fatal. This reaction consists of the activation of existing luetic lesions following the initial administration of a spirochetocidal agent such as an arsenical drug or penicillin. The reaction is characterized by vasodilatation and edema at the site of a lesion. In a patient having partial coronary osteal stenosis due to syphilitic aortitis, the edema may produce further narrowing of the coronary ostium or complete coronary occlusion may occur. The result may be an anginal syndrome, heart failure, or death. The same clinical picture, though somewhat delayed, may result from therapeutic paradox. When aneurysm of the aorta is present it is said that a treatment reaction may result in further dilatation of the aorta or even in its rupture, but the author has never seen the latter.

All physicians recognize that the arsenical drugs are strong spirochetocides and that their use may be followed by a Herxheimer reaction. Few, however, think of penicillin as being powerfully spirochetocidal because it is relatively non-toxic otherwise. Penicillin is a powerful spirochetocide and because of this should be used cautiously in patients having

From the Department of Medicine, College of Medical Evangelists, Los Angeles.

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late syphilis unless they have been properly prepared for its use. This fact should be kept in mind whenever penicillin is used in the treatment of any infectious disease, because syphilis may also be present.

When the foregoing facts are understood there can be only two common causes for the occurrence of Herxheimer reactions. The first cause is that cardiovascular syphilis may be present in the asymptomatic form and hence be unrecognizable, and this might lead to a diagnosis of latent syphilis and over-intensive treatment. The second cause is that the physician may not examine the patient carefully enough to discover obvious cardiovascular syphilis. Unfortunately this latter cause is responsible for the majority of Herxheimer reactions.

Severe reactions can be almost completely avoided by careful clinical study of every patient before any antiluetic treatment is given and by starting the treatment with adequate courses of heavy metal when cardiovascular involvement is found or is even suspected. Every patient who is to be treated for syphilis should be subjected to a complete history taking and physical examination, and ideally should have a careful roentgen study of the heart and aorta. If this is done, most cases of complicated aortitis will be found. Serious reactions may be avoided in treating uncomplicated and hence undiagnosable aortitis by starting treatment in all patients having late syphilis with a long course of a mildly spirochetocidal drug such as bismuth.

THE ACTIVE TREATMENT OF CARDIOVASCULAR SYPHILIS

The anginal syndrome or cardiac failure when due to aortitis and its complications should be treated as they would be treated in any patient regardless of the cause. Antiluetic treatment should be withheld from patients who are in cardiac failure due to cardiovascular syphilis.

When cardiovascular syphilis has developed to the point where it can be diagnosed, it is commonly undertreated. This unfortunate state of affairs is almost always attributable to the physician's fear of the Herxheimer reaction and its consequences. The reaction need not be feared if the physician knows that the patient has cardiovascular syphilis and treats him properly. No patient being treated for cardiovascular syphilis at the White Memorial Clinic during the last ten years has experienced a Herxheimer reaction, in spite of the fact that we employ larger and more numerous doses of the arsenical drugs than have heretofore been advocated in the literature. This is probably due to the fact that all our patients have been carefully prepared for the use of the powerful spirochetocides.

A number of serious treatment reactions involving the cardiovascular system have been seen. Patients with severe reactions were sent to us by physicians who in most instances had not examined their patients before starting treatment, and hence were unaware of the existence of cardiovascular syphilis. Treatment with arsenical drugs had been started before the patients were properly prepared. The moral is: Know the patient and then treat him carefully but adequately.

The proper approach to the specific antiluetic treatment of cardiovascular syphilis is a long course of heavy metal which is but mildly spirochetocidal. Bismuth subsalicylate in oil may be given each week for 12 to 16 weeks in doses of 130 mg. to 200 mg.

The iodides seem to be useful in syphilis as in most other granulomatous diseases. Many syphilotherapists start iodides at the onset of bismuth treatment, but the author prefers to wait four to six weeks and then start using saturated solution of potassium iodide in doses of 15 drops three times daily after meals. The dosage is increased gradually so that after about four weeks the patient is taking 60 drops three times daily. Iodides are given with each course of bismuth.

The patient who has cardiovascular syphilis is benefited very little, if at all, by antiluetic treatment unless arsenical drugs are used. The postmortem studies done by Howe[1] demonstrate that there is just as much cellular infiltration in the aortas of patients treated with large amounts of heavy metal as there is in untreated patients. He also showed that there was very little celluar infiltration in the aortas of patients who had received as few as 12 arsenical injections. This demonstrates the need for arsenic and the futility of using bismuth and iodides alone.

After proper preparation with bismuth and iodide, arsenical medication should be cautiously started. The newer arsenical drugs, the arsenoxides, are preferable to the arsphenamines. Mapharsen is the most widely used. The initial dose of mapharsen in common use at present is 10 mg., but the author prefers to use 1 mg. in order to minimize the chance of a Herxheimer reaction. The second dose is usually 5 mg. if the patient has no reaction after the first. The injections are given weekly and may be increased by 5 mg. each week until a dose of 60 mg. is reached. Before each treatment the patient should be questioned to determine if the preceding treatment was followed by angina, dyspnea, tachycardia, palpitation, etc. If any cardiac embarrassment has been experienced the dose must be materially reduced, and then increased more gradually than before. The injections may be given weekly until 20 have been given in the first course. Because the first six doses of mapharsen are very small it is a good plan to give the patient bismuth injections simultaneously.

Most syphilologists recommend that the dose of mapharsen be limited to 30 or 40 mg. Our experience at the White Memorial Clinic during the last ten years causes us to believe that such doses are needlessly small and that they decrease the efficiency of the treatment. Practically all our patients have been given 60 mg. of mapharsen weekly after having been slowly worked up to this dose.

My colleagues in the clinic in treating their patients have used courses of ten weekly injections of bismuth alternated with courses of ten or twelve

weekly injections of mapharsen. My patients have been given mapharsen in courses of 20 weekly injections alternated with courses of ten weekly injections of bismuth. Treatment is given for three or four years continuously.

No serious treatment reaction has been encountered on the vigorous program of treatment described. All our patients seem to have been definitely benefited. None have shown evidence of progression of the syphilitic process in the cardiovascular system. The disease appears to be arrested for the time being at least.

Penicillin is powerfully spirochetocidal and presumably will prove to be useful in the treatment of cardiovascular syphilis. However, it is so new a drug that it has not yet been possible to evaluate it, and consequently its use might well be left to large clinics where it can best be studied. Its ability to produce severe Herxheimer reactions should always be kept in mind.

CONCLUSION

1. Cardiovascular syphilis may be almost completely prevented by adequate treatment of early syphilis or even of late latent syphilis.

2. Serious treatment reactions as a rule occur only when patients are given powerful spirochetocidal drugs before being adequately prepared for them by long courses of the mildly spirochetocidal drugs.

3. The physician is usually unaware of the presence of cardiovascular syphilis in the patient who develops a Herxheimer reaction due to overtreatment. This unawareness may be due to the fact that uncomplicated aortitis, and some of the partially developed forms of complicated aortitis, are not disagnosable. Frequently, however, obvious cardiovascular syphilis is overlooked because the patient is not adequately examined. Too many patients are given antisyphilitic treatment as soon as a positive reaction to a serologic test for syphilis is found, even though they have been examined only superficially, if at all.

4. When cardiovascular syphilis is diagnosed it is usually undertreated because the physician fears the Herxheimer reaction. This reaction need not be feared if the patient is properly prepared for the powerful spirochetocides.

5. Adequate doses of the arsenical drugs are essential to satisfactory treatment results.

6. Penicillin has not been adequately evaluated to be routinely used in the treatment of cardiovascular syphilis. It is capable of producing severe Herxheimer reactions.

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Intraocular Foreign Bodies in Naval Personnel

Hugo Lucic, M.D., *San Diego*

PENETRATING wounds of the eyeball with lodgement of one or more foreign bodies within its deep structures were one of the more important types of injuries seen in navy personnel during the recent war.

Most of such injuries in patients admitted to one of the naval hospitals on the Pacific Coast were incurred in either (1) action against the enemy or (2) at work or in military training, usually in the vicinity of the hospital. Patients wounded in combat usually did not reach the hospital at which the author was stationed until several weeks following the injury and some of them already had received expert care at one or more hospitals along the route. Those injured in the proximity of the hospital, however, usually were seen within a few hours following the accident.

From January 1941 to July 1946 some 95 patients presumably with intraocular foreign bodies were admitted to the hospital. The records of 68 of these were analyzed.

Of the 68 patients with intraocular foreign bodies 40 received injuries in combat and 28 in the course of work or military training. In 35 of the 40 men injured in action the foreign particles in the eyes were presumed to be nonmagnetic. The particles in the remaining five were magnetic. Ten of the 40 men who were injured in action had multiple particles within the same eye and three suffered injury to both eyes. In three of the five cases in which the particles were magnetic they were successfully removed. In two cases the eyes had to be enucleated. A large number of the nonmagnetic particles were small, and as they were apparently well tolerated they were left undisturbed.

Of the 28 men who received injuries at work or in the course of training, 21 harbored magnetic particles, and in 17 of the cases these were successfully removed. In five of the seven cases in which the particles were nonmagnetic, the particles were removed. In three of the 28 cases the affected eye had to be enucleated.

DIAGNOSIS

History. In making a diagnosis of intraocular foreign body a careful history of the injury is of considerable importance. An eye that was injured while the man was exposed to flying particles of hand grenades, land mines, bombs, machine gunfire, or other flying missiles, or while the patient was hammering, drilling, etc., should be suspected of harboring a foreign particle. A careful description of the tools used and the manner in which the accident occurred help to determine the probable nature of the foreign body.

Clinical Examination. Often the wound of entrance, which may or may not be associated with prolapse of the uveal tissue or vitreous, can be seen by ordinary examination. On the other hand, the wound may be so small as to be invisible even with the aid of the slit lamp and corneal microscope. A reduction in intraocular pressure, a shallow anterior chamber, or hemorrhage in the vitreous and lenticular opacities are signs which point to an ocular perforation and the possibility of an intraocular foreign body.

In old injuries the chemical effect of the foreign body may be visible. Fragments of copper produce specific changes known as ocular chalcosis. These are seen as a peculiar greenish color in Decemet's membrane and lens capsule, and the changes in the latter produce a picture simulating a sunflower. Steel or iron retained in the eye over a long period slowly oxidizes and the products of oxidation stain the ocular tissues a reddish-brown known as siderosis. This is usually seen clinically in the lens, iris and cornea.

The following case is an example:

CASE REPORT

A carpenter's mate, aged 21, entered the hospital February 22, 1944, complaining of impaired vision in the right eye. He stated that in 1940 while he was pounding on a nail a piece of steel hit his right eye. He received medical treatment for nine days, and the eye then was apparently well. No x-ray examination was made at the time. On admission to the hospital vision in the right eye was limited to counting of fingers at six inches. The iris appeared greenish-brown in color and there were several dark brown granules dispersed through the subcapsular region of the opaque lens, giving it a dirty-grey appearance and indicating siderosis (Figure 1). Intraocular tension was normal. Roentgen examination revealed a small (1 mm.) metallic particle in the region of the ciliary body. The particle was removed by the anterior route through a small corneal incision. The lens was subsequently needled and final corrected vision was 20/20.

X-ray Examination. An x-ray examination is indicated whenever there is suspicion that a foreign body has struck the eye even though a careful clinical examination reveal no sign of injury. Small foreign bodies may not show in an x-ray film taken in one view only. In such instances several different exposures should be made, as advocated by Thorpe.[5] When a particle is not entirely radiopaque or is so small as not to show against the shadows of the bones, it can sometimes be demonstrated by the bone-free method of Vogt[2] provided it is located in the anterior segment of the eye. This is accomplished by using small

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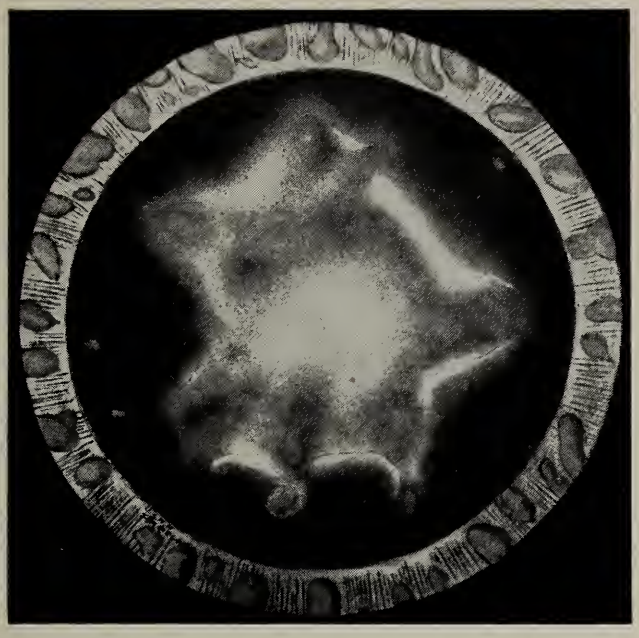


Figure 1.—Iris and lens showing siderosis.

dental films pushed deeply into the orbit at the nasal angle, with the orbit then photographed from an anterolateral position. To obtain a better exposure the eye may be made to protrude by retrobulbar injection of 3 cc. of a 1 per cent solution of procain hydrochloride.

Localization. Before extraction of a foreign body from the eyeball is attempted, its exact position in relation to the globe should be determined. This is imperative if the particle is nonmagnetic, less important if it is magnetic and its size and shape known.

There are several satisfactory methods of localization. We have employed Comberg's method.[3] A contact lens with four lead marks is placed over the cornea and two exposures are made, one exactly in the visual line (Figure 2) and one at right angle from the first exposure (Figure 3). Location of the foreign body with reference to the central point then is easily determined by drawing lines between the shadows of the marks on the plate. The meridian of the globe is found by extending the line from the foreign body to the central point to meet the horizontal drawn on the chart and the distance of the particle from the plane of the limbus is easily determined in

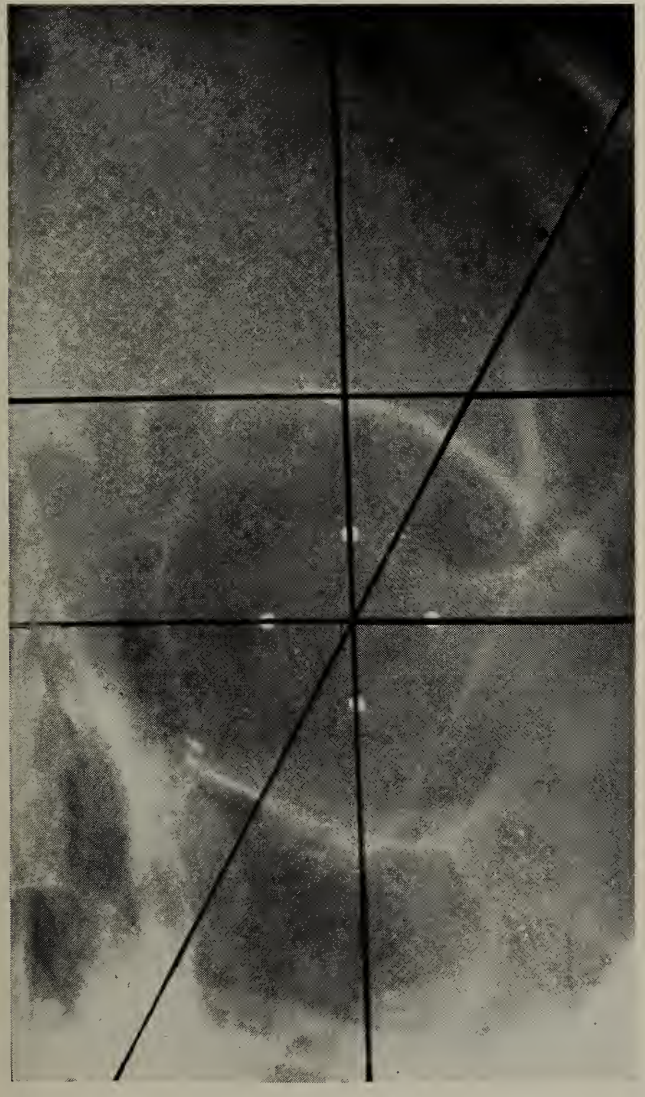


Figure 2.—Roentgenogram with lines for localization of foreign body in frontal plane according to Comberg.

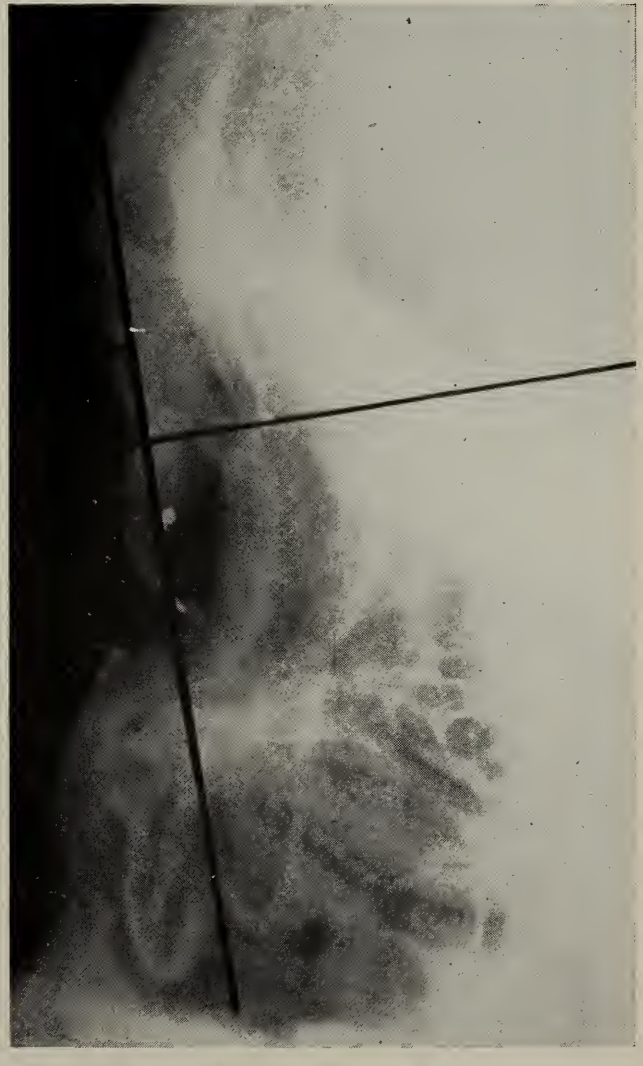


Figure 3.—Lateral view.

the lateral view. The results are then plotted on special charts (Figure 4).

Comberg's method is highly satisfactory in most cases, but occasionally error creeps into the picture and the foreign body is localized 1 or even 2 mm. from its true position. This, of course, is a serious mistake when dealing with nonmagnetic particles or when a particle is close to the periphery of the globe so that it appears to be extraocular when it is actually in the eye, or vice versa. The latter difficulty can often be eliminated by injecting air into Tenon's space to create a contrast between the globe and the surrounding tissue. The chief objection to the Comberg lens is that it sometimes slips off the cornea, thereby introducing a serious error in localization. Thorpe[6] has recently modified the Comberg lens to obviate this objection by drilling suture holes in the periphery of the lens so that it can be anchored.

If more than one foreign particle is present, and especially if one is imposed upon another, localization of each in reference to the globe may be difficult or even impossible. The following case report is illustrative:

CASE REPORT

The patient received injuries about the face and both eyes due to a hand grenade explosion. A small particle of shrapnel was removed from the left eye at another hospital. Eight weeks later, on admission to the hospital at which the author was stationed, vision in the right eye was 20/200 and in the left eye 20/20. Except for a small corneal scar, an anterior synechia, and an irregular pupil, the left eye appeared normal. The right eye presented a grey, organized mass in the lower part of the fundus and a hazy vitreous. Roentgen examination disclosed several metallic particles in the region of the eye, two of which, although appearing to be within the globe, were difficult to localize because of multiplicity of shadows in the two views.

A foreign body in the vitreous which shifts with the position of the head presents another problem in localization. Two such cases were seen among the 68 patients. In one of these the particle was magnetic and the lens was already opaque. It was easily extracted by the anterior route. In the second the particle, which was visualized through the pupil, moved freely in the vitreous with each movement of the eye. It was nonmagnetic and it was removed with a forceps under direct visualization.

TREATMENT

It may be stated categorically that any intraocular foreign body should be removed as soon as possible unless its removal involves more danger than its retention in the eye. Details of the surgical procedure and medical treatment will depend on several factors, such as the age and extent of the injury, the size, shape, nature and location of the particle.

If the injury is recent, the patient is given prophylactic doses of sulfadiazine or penicillin and injections of typhoid antigen intravenously. Antitetanic serum is often indicated. Atropine is used in most cases unless contraindicated by primary glaucoma.

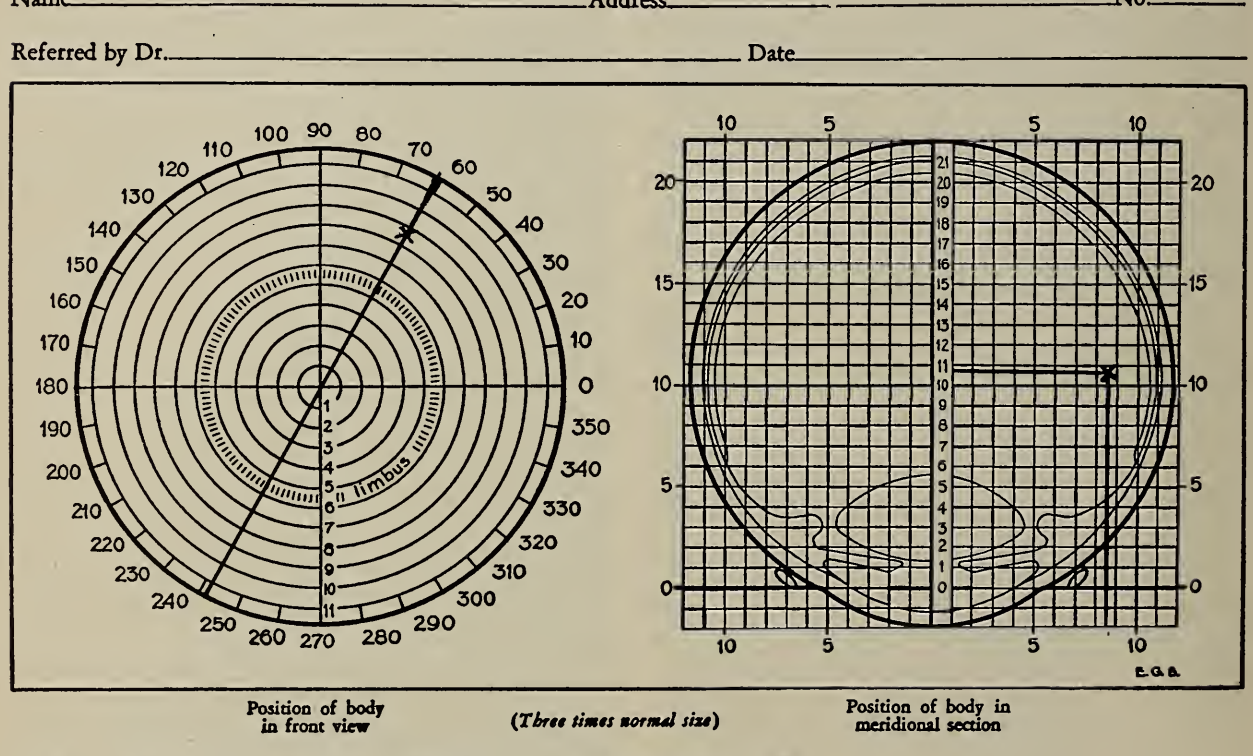


Figure 4.—Comberg's charts for plotting localization in the two views.

If severe intraocular infection develops, with loss of light projection, removal of the eye is advisable.

As magnetic foreign bodies usually can be removed without difficulty while nonmagnetic particles present an entirely different problem, it is important to know before operation whether the particle is magnetic or not. Theoretically a radio-amplification device, such as the Berman Locator[4] would be an ideal instrument to use in cases of doubt. If such an instrument is not available, other methods of differentiation must be used. As patients with shrapnel injuries of the eyes usually had similar particles imbedded about the face, these were removed and tested for magnetic reaction. In the absence of such particles we had to resort to the use of the magnet for differentiation.

Magnetic particles may be removed by the anterior or the posterior route, the choice depending on the size and shape of the foreign body and the damage suffered by the eye. The author believes that when the foreign body is small, when a cataract is already present or when the particle is located in the region of the macula, the anterior route should be used, and that large, jagged particles should be removed by the posterior route, especially if the lens is clear.

In extracting foreign bodies by the anterior route the giant magnet is used and exact localization is not necessary. The pupil is dilated widely and the magnet is applied first at about 12 inches from the cornea, using the least amount of current available. The current is turned on intermittently and is increased gradually. The magnet also is slowly brought closer to the cornea. If the foreign body is attracted by the magnet the iris is seen to bulge forward and the patient will usually experience some pain. By careful manipulation of the magnet the particle is brought into the anterior chamber and is then extracted with the hand magnet through a corneal incision. The corneal incision should be so made as to avoid the formation of a large shelf. This can be accomplished more easily by using a cataract knife rather than a keratome.

Sometimes magnetic particles can be extracted by the anterior route several years following the injury. (Case 1, Figure 1.)

Extraction by the posterior route requires an incision in the sclera usually as near the foreign body as possible unless there is a fresh scleral wound already present. The incision should be meridional and large enough to allow the largest diameter of the particle to pass freely. If the incision need be large, an intrascleral suture should be inserted before completion of the incision. To prevent retinal detachment, diathermy coagulation should be employed around the incision. When the particle is in the vitreous, an equatorial incision may be made over the flat portion of the ciliary body to avoid making a hole in the retina as advocated by Verhoeff[7] or a trephining hole as used by Barbour and Fralick.[1] The incision may be made also at the ora serrata along the anatomical attachment of the retina. The tip of the hand magnet is then introduced into the eye for a distance of about 2 mm., the current is turned on and the particle extracted. After extraction of any intraocular foreign body, atrophine is used, the eye is covered and the patient is kept quiet for several days. The following case illustrates this method of extraction:

CASE REPORT

The patient was hit in the left eye by shrapnel. On admission to the hospital a month later, vision in the left eye was 20/40. There were no external signs of injury but the vitreous presented a particle which appeared to be a foreign body. The lens was clear. X-ray examination showed an intraocular, metallic foreign body measuring approximately 2 mm. in diameter and located in the 62 degree meridian in the superior temporal quadrant, 8.6 mm. from the visual axis and 10.6 mm. posterior to the limbal plane (Figures 2, 3 and 4). The sclera was exposed in the indicated region, an equatorial incision 4 mm. long was made half way through the sclera 10 mm. from the limbus, a mattress suture was inserted and the incision was completed to the choroid. Diathermy coagulation was used around the incision and the choroid was incised with a sharp cataract knife. The tip of the hand magnet was inserted into the wound, the foreign body was extracted without difficulty and the incision was closed. Subsequent progress was uneventful and the vision remained 20/40.

Nonmagnetic particles when visible in the anterior chamber may be extracted with special forceps through a corneal incision. Similar particles in the posterior segment are difficult to remove and it is often less dangerous to leave them undisturbed than to attempt their removal. Small particles of glass and other inert substances are often well tolerated by the eye and may be retained for many years without much damage to vision. We have left undisturbed a majority of the eyes harboring tiny particles of nonmagnetic shrapnel which had not caused any reaction during the period of observation of six months or longer.

Particles of copper are notoriously poorly tolerated and whenever possible should be removed. Such particles when visible in the vitreous may be removed with special or improvised forceps, as illustrated by the following case:

CASE REPORT

The patient received an injury to the left eye when a copper blasting cap exploded in his hand. Vision in the injured eye was 20/70. The vitreous was somewhat hazy due to the presence of blood, but a tiny, glistening particle, presumed to be copper, could be seen floating in its anterior portion. The anterior chamber and intraocular pressure were normal. There was no visible evidence of a wound. Roentgenograms did not show evidence of an intraocular foreign body, but two particles were present in the soft tissues. Application of the giant magnet did not attract the intraocular particle. Two days after the injury the blood in the vitreous had absorbed sufficiently to allow good visualization of the foreign body.

The particle was removed with a Kalt capsule forceps after obliterating the curve of the forceps. The sclera of the superior temporal quadrant of the globe was exposed, a small equatorial incision was made halfway through the sclera in the region of the ora serrata, a suture was placed through both lips of the incision and the incision was completed into the vitreous. The forceps was introduced into the vitreous and under direct visualization the particle was

grasped and extracted. It proved to be a particle of copper measuring 1 mm. in diameter. The patient was given prophylactic injections of typhoid antigen intravenously and sulfadiazine orally. He was discharged from the hospital three weeks later with visual acuity of 20/20. Three months following the injury vision was 20/15 and the eye appeared normal.

Large particles of copper when embedded in the deep structure of the eye will certainly cause subsequent reaction and should be removed. The following case illustrates this point and shows how a large particle may be removed from the ciliary body:

CASE REPORT

The patient was struck in the right eye by a piece of wire. He was treated at the time and when the eye was free of inflammation was discharged to duty with vision of 20/20. According to the history an x-ray examination at that time revealed no foreign body. Approximately six months later, vision gradually became blurred and the patient was admitted to the hospital 15 months following the accident. Vision in the affected eye was limited to ability to distinguish hand movements. There were cells in the anterior chamber, and the lens was opaque and dislocated. Intraocular pressure was normal. X-ray examination disclosed a foreign body 11 mm. long located in the inferior temporal quadrant, in the ciliary body, somewhat concentric with the limbus (Figure 5). A meridional incision 5 mm. long was made over the foreign body which was engaged with a blunt iris hook and extracted.

Occasionally an intraocular foreign particle may spontaneously work out to the surface through the original wound or through the surgical incision following an unsuccessful attempt at removal, as illustrated by the following case:

CASE REPORT

The patient was hit in the eye by a particle of shrapnel. He entered the hospital eight weeks later, at which time vision in the injured eye was 20/70. X-ray examination disclosed a metallic particle in the inferior temporal quadrant, 6.8 mm. from the visual line, 3.2 mm. posterior to the limbus (Figure 6). Details of the fundus could not be made out due to the presence of blood in the vitreous. The indicated area was exposed, a 5x2 mm. scleral flap was raised and the hand magnet applied over this area, without success. The reaction in the eye subsequently quieted and vision improved to 20/40. Six months later, the particle was seen to bulge under the conjunctiva and it was removed with a forceps. It was nonmagnetic.

Undoubtedly many nonmagnetic particles may be successfully removed from the eye with the aid of the biplane fluoroscope or the ocular endoscope, but the author has used the former in one case without success and has had no experience with the ocular endoscope.

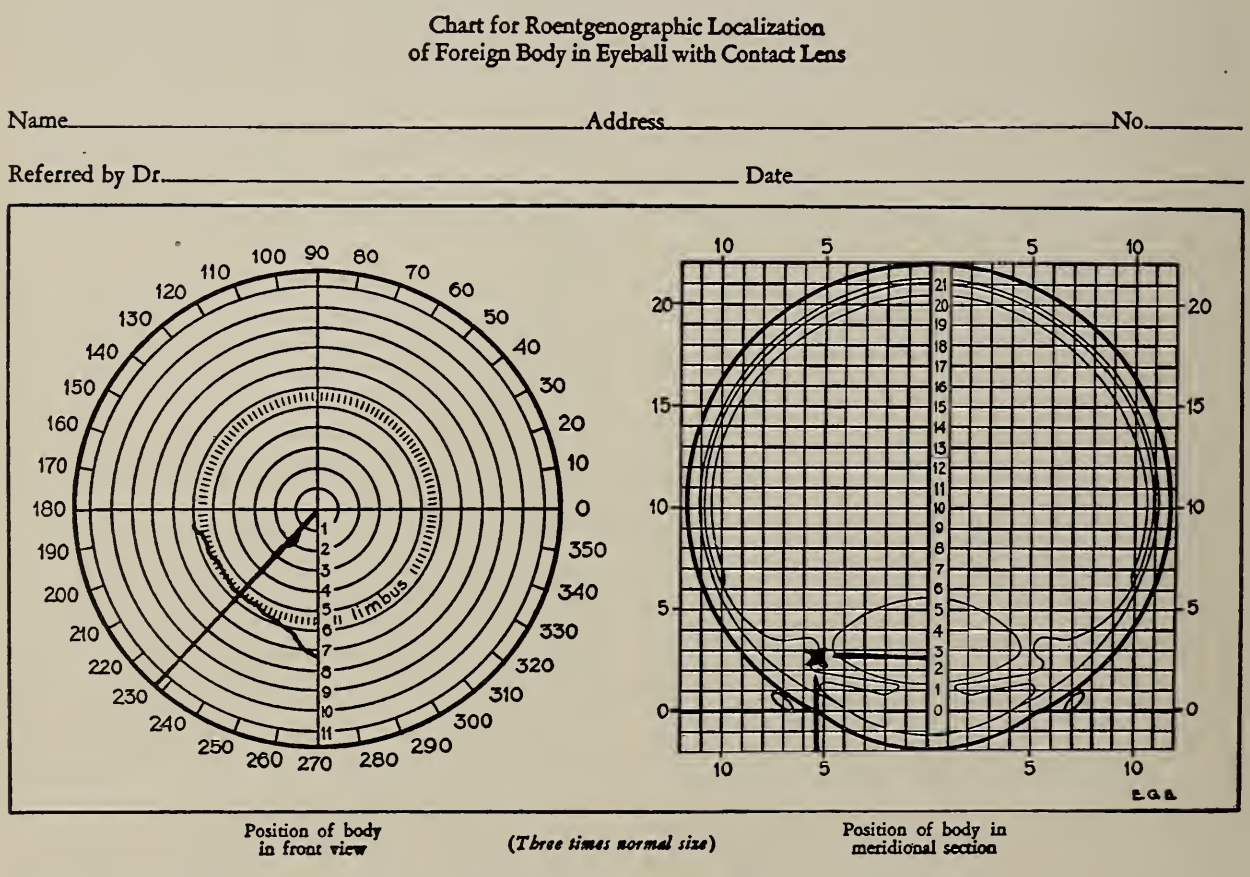
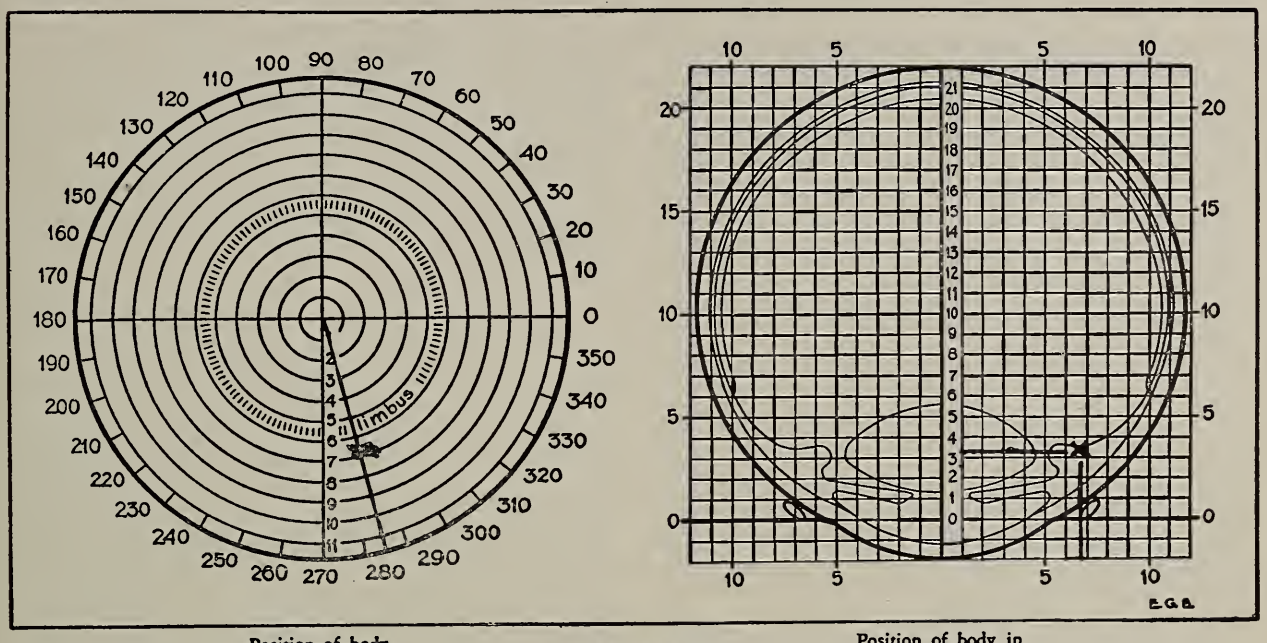


Figure 5.—A long piece of copper wire localized in the ciliary body.

Chart for Roentgenographic Localization of Foreign Body in Eyeball with Contact Lens

Name_____ Address_____ No._____

Referred by Dr._____ Date_____



Position of body in front view (*Three times normal size*) Position of body in meridional section

INFERIOR TEMPORAL QUADRANT, LEFT EYE. 284 DEGREE MERIDIAN.
6.8 mm. FROM AP AXIS. 3.2mm. POSTERIOR TO PLANE OF LIMBUS. 1mm. IN DIAMETER.

Figure 6.—Nonmagnetic foreign body localized in the ciliary body, worked out spontaneously.

Small foreign bodies located in the crystalline lens, if nonirritating, like a piece of glass or aluminum, should be left undisturbed as they may not cause progressive opacification. A patient was admitted to the hospital three days following multiple injuries received in combat. In the cortex of the left lens, just above the center, there was a glistening particle which was presumed to be aluminum. The path made by the particle could be traced through the eye by the scar in the cornea, the hole in the iris and the anterior capsule of the lens. Vision in this eye was 20/40. The particle was considered nonmagnetic and no attempt was made to remove it. Six months later vision in this eye was 20/20 and there was no sign of active inflammation in the eye.

Any penetrating injury of the eye is a potential cause of sympathetic ophthalmia. It is remarkable that not one case of this dread disease has occurred among perhaps 150 patients with penetrating injuries that were observed during the entire war at one of the largest naval hospitals.

1006 Medico-Dental Building.

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Environmental Survey in the Diagnosis of Allergic Disorders

NORMAN SHURE, M.D., *Beverly Hills*

A SURVEY of the patient's environment is a necessary although frequent minimized adjunct in the diagnosis of allergic disorders. This involves a consideration and evaluation of possible pertinent allergic offenders in the patient's immediate surroundings. In most practices this information is secured by questioning the patient during the initial interview. However, in the experience of the author, this procedure is unsatisfactory because the patient often is unaware of the details of his environment without preliminary study and thought. Patients, as a rule, do not know the composition of their upholstered furniture, mattresses and pillows; they cannot identify trees and weeds in the neighborhood of their homes; they do not know the exact ingredients of the vitamin pills they take or of the canned food they eat. In a seasonal pollen allergy these details may not appear important, but in an obscure perennial rhinitis, persistent asthma or prolonged atopic eczema, they may be critical.

A more satisfactory method of obtaining the required data, we have found, is to submit a detailed questionnaire to the patient for completion at home after consultation with other members of the family and examination of manufacturers' labels on household articles. The ideal method, one that we have found to be increasingly necessary in our clinic, is that of the physician or a trained member of the staff visiting the patient's home and making a detailed inventory of the environment, searching for allergens which may be related to the patient's complaint. It is the purpose of this paper to outline a systematic method of conducting such a survey and to discuss in some detail the factors involved. The plan outlined in this discussion may be made the basis of a questionnaire for the patient to complete, or may be used as a guide by the person actually making the physical survey.

NEIGHBORHOOD

The location of the house is very important. The house on a busy thoroughfare with much traffic on it will be subjected to invasion by fine dust particles, while one situated in the center of a four-acre wooded tract will be invaded by tree, grass and weed pollens. The author recalls at least one case in which the patients' asthma was immediately relieved when he moved from a neighborhood in the vicinity of a furniture factory. Another patient was cured of a constantly running nose when she moved from a neighborhood near a railroad track along which an average of 12 smoke-belching locomotives passed daily.

The importance of identifying trees, weeds and grass in the vicinity of the home is well known. Allergic symptoms of one patient were immediately ameliorated when the weeds on a vacant lot adjacent to her home were burned. Another patient with olive tree sensitivity was surprised to learn that the magnificent tree on her front lawn was an olive and was quite pleased when her symptoms disappeared on its removal.

If the patient lives on a farm one must consider the crops planted and should search for rusts and smuts.[6] A farmer with severe hay fever during the threshing season was greatly relieved of his symptoms by hyposensitization with corn smut. Recently the author had occasion to study a farmer with asthma who was found sensitive to an autogenous dust extract prepared from dust collected in his barn. Having the patient avoid the barn as much as possible and treating him with the barn dust produced great relief of symptoms. Animals encountered on the farm, too, should not be overlooked. Last year the author studied a dairy farmer who was exquisitely sensitive to cattle hair. This case posed a problem which was solved by change in occupation.

THE HOUSE

The age and state of repair of the house, the author finds, is a factor which the patient and many doctors overlook. A damp house with decayed wood in its framework is likely to be a cause of trouble especially in mold-sensitive patients.[1] Most patients cannot associate common mildew with their allergy. Some time ago the author interviewed one patient who had traveled and lived in all sections of the country in search of a warm spot where, he felt, his asthma would be better. This patient could not understand why his asthma was worse in Florida until it was pointed out to him that he was sensitive to fungi which were prevalent in that tropical climate. In another case seen by the author, the patient's hay fever was at its worst in the autumn when the heating system of his house was used for the first time. The cause of the disease became obvious when a visit to the home revealed a very damp basement with rotted wood piled up in it and a very efficient forced air heating system which disseminated clouds of fungi into the patient's bedroom. The method of cleaning the house, too, may be a deeply rooted habit and appear unimportant to the patient. Thus an associate reports a miraculous cure in a patient by mere substitution of a vacuum sweeper for a broom.

BEDROOM

After considering the neighborhood and the general aspects of the house, the next step is to examine individually the important rooms within the house.

Assistant Professor of Internal Medicine, College of Medical Evangelists.

From The Allergy Clinic, The White Memorial Hospital, Los Angeles.

Because the patient spends more consecutive hours in it than in any other room in the house, our practice is to survey the patient's bedroom first. Dust as an antigen in the production of allergic symptoms is well known,[3] but few people realize that it can be found in such hidden and overlooked spots as tops of windows and door casements, curtains and drapes, the edges of rugs, venetian blinds, pictures, wall brackets, knick-knacks and candelabra. Dust often lurks in the coils of spring mattresses, behind dressers and on steel beds. Our practice has been to inspect the room much as a Navy officer does during his weekly inspection, running a finger over inaccessible and overlooked areas in search of dust. In our experience, the most common hiding places of dust in bedrooms are in the coils of bedsprings and in closets where seldom-used clothes hang.

Wool is another allergen that is common as a cause of allergic symptoms. That blankets are woolen is well known to most patients, but it is not so commonly known that common domestic rugs are made of wool. Both can produce symptoms. One patient recently was relieved of major symptoms by substitution of a cotton rug and removal of several wool sweaters found hanging in the closet. Rug and carpet pads are usually made of cattle and horse hair or of jute. As all are capable of producing symptoms they may have to be eliminated. Chenille rugs often contain cow hair while Chinese and other oriental rugs are combinations of wool, cow hair and even dog hair.

Mattresses, which are usually made of cotton linters, horse hair and pig hair, may cause symptoms in a patient. The common "inner spring" mattress is primarily composed of cotton linters. These are usually inadequately covered and, especially if old, can be the cause of symptoms. Some time ago in our clinic we cultured a series of fragments of cotton removed from inner spring mattresses and obtained almost pure cultures of several fungi.

Pillows, of course, are filled with feathers. The more expensive pillows are filled with down (goose feathers) while the less expensive are filled with varying proportions of chicken, duck and turkey feathers. The age of the pillow should be considered. On exposure of a Petri dish alongside a bed overnight we were able to identify feathers in surprising quantities. Culture of this material on enriched medium resulted in a lush growth of molds. One can readily see what effect a good night's sleep on a soft old feather pillow will have on a patient sensitive to feathers or mold. Kapok, too, we found by similar investigative methods was not only a good allergen, but also an excellent medium for fungus growth.

LIVING ROOM

In the living room also the dust problem must be scrutinized and the hiding places examined. Fireplaces which are not cleaned often are great repositories of dust. As in the bedroom, rugs, rug pads and furniture upholstery materials must be considered. Furniture covering may be any of a number of materials, the most important from the allergist's point of view being wool and mohair. Mohair is made of goat hair and is a common constituent of plushes, velvets and velours. Silk which may be used in cover ing furniture should not be overlooked as a cause of allergy. In considering silk one should not be misled by such terms as faille, satin, foulard, pongee, taffeta and jersey, which are all primarily silk.

The obvious question at this point is, "How is one to know what the living room furniture is made of?" The author made a visit to a major furniture store recently and examined manufacturers' labels on upholstered furniture and mattresses. Many states have laws requiring the manufacturer to attach a tag to each article of such furniture stating the exact composition of the concealed materials used in its manufacture. Thus a typical label on a couch read, "Concealed Materials Are All New Materials. Contents: Body—Horse Hair, 12½ per cent; Hog Hair, 87½ per cent, together constituting 50 per cent Cotton Felt, 50 per cent Cushions—Duck Feathers 75 per cent, Down 25 per cent." If there are no tags, or if the patient had removed them on purchase, the general composition as outlined here will fit most articles. The importance of the composition of upholstered furniture was recently brought to the attention of a member of our clinic whose patient, sensitive to hog hair, was relieved of symptoms upon buying a new couch.

The fireplace should be scrutinized carefully, not only for dust but for the type of wood burned. A former associate, some years ago, reported a case of severe asthma resulting from wood smoke.[4] Other factors which one looks for in the living room are artificial leather on furniture and heavy coating of furniture polishes and waxes. These all may contain large amounts of linseed oil, which is not an unusual cause of allergy.

BATHROOM

A list of all the drug and toilet articles found in the medicine cabinet should be made because patients too often forget the medicines they take and the cosmetics they use. Hair brushes, shaving brushes and tooth brushes should be considered in the light of possible animal hair allergy. One patient who was sensitive to animal hair had his entire allergy problem solved by mere substitution of an electric razor. Common proprietary medicines and toilet articles may contain an allergic ingredient of which the patient is not aware. Orris root, an important allergen, is no longer a common constituent of face powders since its allergic importance has been pointed out to cosmetic manufacturers. However, it is still used as a carrier or binder for odors in perfumes and therefore may be found in perfumed toilet articles. The so-called allergen-free cosmetics and face powders are mainly free from orris root and therefore may be as allergenic as most of the commercial powders. The importance of hidden ingredients in medicines was brought to the attention of an associate very strikingly when a patient, exquisitely sensitive to milk, continued to have asthma

in spite of a rigid milk-free diet. In this case it was discovered after prolonged investigation that the ephedrine and aminophyllin capsules prescribed for symptomatic relief contained lactose.

Powder puffs may contain sheep or lamb wool, though the majority of the inexpensive ones used by most women are made of cotton. Linoleum on bathroom floors is commonly treated with linseed oil, and in some cases an oiled silk shower curtain may be the cause of the trouble.

KITCHEN

A list of all the foods in the kitchen cupboards and in the refrigerator should be made, mainly because the patient forgets what he eats. Patent prepared and packaged foods must be suspected primarily because of the hidden allergens they contain. Although manufacturers' labels required by food and drug laws are adequate, patients are not label-conscious and actually do not know what they eat. A discussion of the hidden constituents in packaged foods could be almost limitless. Several examples, however, are in order and will serve the purpose of emphasizing their importance. Corn, in the experience of the author, is the most ubiquitous allergen found in commercially packaged foods. It is used in almost all syrups, candy bars, ices, sherbets, ice cream, tenderized ham, canned fruits and baking powder. Corn is used in chewing gums, in bourbon and other whiskies, in beer and ale, and in carbonated beverages. Unless there has been a change in formula recently, such well known products as Welch's Grape Juice, Jello, Mull-Soy, Pablum, Linit, Kix, Mazola and Karo contain corn products. Wheat, egg and milk sensitivity are the most common and the detection of these ingredients in commercial food products often is difficult. A visiting lecturer, some years ago, described a patient who was sensitive both to coffee and to wheat. This patient used Postum as a substitute for coffee and continued to have symptoms until it was discovered that Postum contained wheat.

Other common allergens found in kitchens are oilcloth and artificial leather which are treated with linseed oil. Brushes and brooms are made of wheat, rye, barley and rice (straw) and of animal hair, mainly that of hog, horse, goat, sheep, and camel. Laundry starch is made primarily of corn, but may be made of wheat or rice. Candles are usually made of cottonseed oil; twine and rope are made of animal hair, cotton linters, straw and flaxseed.

CLOSETS

Closets have already been mentioned as repositories of dust. In many homes closets serve as catchalls and therefore may contain any number of possible allergens. Fur coats and fur collars on cloth coats should be regarded with suspicion and the fur must be identified. It should be pointed out that rabbit pelts are commonly plucked, sheared and dyed in imitation of more expensive furs such as seal, fox, squirrel, mink, beaver, leopard, and sable. These imitations usually parade under trade names with the suffix "ette" or "ine" added such as Beaverette and Squirreline; or they may be identified by the addition of modifying proper names, becoming Belgian beaver, French leopard, French sable and Australian seal. The author recalls one case in which a lifelong friendship was almost terminated when it was pointed out to a patient in the presence of a friend of hers who wore a French beaver coat, that a sensitivity to rabbit hair caused her symptoms to develop in her friend's company.

Among the articles commonly found in closets which may be related to the patient's allergy are felt hats, commonly made of various animal hairs, and patent leather shoes, which are treated with linseed oil. Clothes moths found in the closet of a patient have been reported as a cause of asthma.[3]

MISCELLANEOUS

The plan outlined to this point should be extended to include other important rooms in the house such as den, sun parlor, nursery, work room and music room. A patient with severe atopic dermatitis was cured when he was forbidden entrance into a workroom where his son made furniture as a hobby. The author remembers a patient with a sunroom filled with plants. The only difficulty was that the patient had an eczematous sensitization to philadendrum. In this connection the author remembers the story a prominent dermatologist enjoys relating about the patient who had an eczematous dermatitis of the hands which was suspected of being caused by a plant in her room, most likely primrose. For more than a year the patient insisted that she had no plants in her home. Finally, after a year of unsuccessful treatment, a new associate in the office asked if she had any plants near her house. "Oh yes," was the glib reply, "I have a primrose plant in a window box just outside my living room which I trim and water every day."

Some miscellaneous allergens do not fit into the plan of room-to-room survey. Among these are paint and plaster walls.[2] Paints and varnishes contain linseed oil or corn oil or both, while plaster often has animal hair incorporated in it. Roofing tar has linseed oil added. Allergy to these is usually to the fresh paint, plaster and varnish rather than to that which has been in place for some time. Painter's asthma is not rare.

Although this is not strictly a part of the physical survey of the environment, mention must be made of the effect of the psyche on allergic symptoms and how a visit to the home may often disclose conflicts which are not apparent during the office examination. During the visit to the home the trained observer may discover the attitude of the patient toward the medical regimen. In the case of a child, one can note the relationship between the child and other members of the family and whether the child is made self-conscious by his running nose, red eyes or wheezing breathing. The author can remember visiting the home of an 11-year-old asthmatic in search of offending allergens. Casually looking at the music

on the piano and noting that there were two sets of almost identical complicated finger exercises, the author was able to ascertain, through questioning, that the patient competed with her elder sister for proficiency in music. Attacks in this case could be directly connected with visits to the music teacher.

SUMMARY

A systematic plan for the survey of the environment surrounding an allergic individual has been outlined and discussed in detail. Though not complete this plan can be made the basis of a questionnaire to submit to the patient, or can be used as a guide by the person making the actual survey.

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Further Experiences With Pontocaine-Dextrose Ephedrine For Spinal Analgesia

A. J. Martinson, M.D., and F. E. Leffingwell, M.D., *Los Angeles*

NOWHERE in the realm of anesthesia is so much accomplished by so little as in spinal analgesia. The few milligrams of drug with which profound degrees of analgesia over extensive areas of the body is achieved would be of inconsequential effect if applied elsewhere. The first spinal injection, consisting of 2 cc. of a 3 per cent solution of cocaine (60 mg.), was given for therapeutic purposes by Corning in 1885.[5] Thirteen years later Bier submitted to the injection of 2 cc. of a 1 per cent solution of cocaine into his own spinal canal.

The dosage of drugs in current use varies with the drug used, the length of the operation and the experience of the anesthetist. In 1928, Sise[9] used from 200 to 300 mg. and occasionally as much as 400 mg. of procaine. In 1935 he introduced the pontocaine-glucose mixture,[10] advocating doses ranging from 10 to 14 mg. for perineal surgery to as much as 20 mg. for procedures in the upper abdomen.

For many years it has been recognized that complications in spinal analgesia are almost directly proportional to the size of the dose of the anesthetic agent. It is not surprising, therefore, that although the quantities of the drug required are now relatively small, efforts should be directed toward developing means of reducing the dosage still further.

Vasoconstrictor drugs were added to the spinal anesthetic mixture very early in the history of spinal analgesia in an effort to prolong the action of analgesia and to make possible the use of smaller doses of the agent. Recent techniques have been introduced by Prickett, Gross and Cullen,[7] who report the use of a procaine-epinephrine mixture resulting in a marked increase in the duration of the analgesia. Their work was based on the well known fact that epinephrine by its vasoconstrictor effect prolongs the action of a local anesthetic agent by decreasing its rate of absorption. The objection has been raised that epinephrine might produce damage to the cord and nerve roots through excessive vasoconstriction and resultant ischemia.[1] This consideration led others to substitute ephedrine since its action as a local vasoconstrictor is not so powerful.[2]

The most recent report on the use of ephedrine intrathecally is that of Potter and Whitacre.[6] They review the work of Jianu and Moisescu[3,4] who in 1932 and 1933 added cardiazol-ephedrine to nupercaine and achieved satisfactory analgesia with as little as 2 mg. of the anesthetic agent. They also cite the work of Romberger[8] who increased the duration of analgesia by 40 per cent or more with mixtures of procaine and ephedrine intrathecally. Potter and Whitacre reported a series of 1,114 patients, half of

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From the Department of Anesthesiology, White Memorial Hospital, College of Medical Evangelists, Los Angeles, California.

whom received pontocaine-dextrose-ephedrine mixture, the other half receiving only pontocaine-dextrose. This report covers only herniorraphies, cystoscopies and operations on the rectum, vagina and lower extremities. They did not use this procedure for intra-abdominal operations.[11] They concluded that ephedrine does prolong the action of pontocaine. Also with this technique it is possible to use smaller doses (as much as 30 per cent less) of pontocaine and still achieve comparable degrees of analgesia, which they felt might increase the margin of safety. These workers noted no untoward effects or serious complication attributable to the use of this combination of agents.

Encouraged by these impressive results, we undertook to determine whether this technique might not be used with benefit in intra-abdominal operations. This presentation is a report of our experience with intrathecal injection of mixtures of pontocaine, dextrose, and ephedrine, in giving 167 anesthetics, of which 103 were for intra-abdominal operations.

TECHNIQUE

In the beginning we followed the technique employed by Potter and Whitacre, i.e., mixing equal parts by volume of 1 per cent pontocaine, 10 per cent dextrose and 5 per cent ephedrine. Using 1 cc. each of these agents results in a mixture containing 10 mg. of pontocaine and 50 mg. of ephedrine in 3 cc. of solution. Therefore, multiplying the required dosage in mg. of pontocaine by 0.3 will yield a figure which represents the number of cc. of solution which should remain in the syringe to be injected into the subarachnoid space without further dilution. In this solution the ratio of pontocaine to ephedrine is 1 to 5.

We started by using doses of 5 or 6 mg. of pontocaine but soon found that in intra-abdominal procedures we were unable to obtain sufficiently high levels of analgesia even when the patient was placed in sharp degrees of the Trendelenburg position. The one exception to this failure is in cesarean section, in which higher levels are notoriously more easily secured with smaller doses than in other abdominal operations. The dosage was then increased to 8 mg., which appeared to be adequate in the majority of cases. In a few cases 10 mg. was given.

In an effort to learn whether or not comparable effects might be secured with smaller dosages of ephedrine, we began decreasing the ratio of 1 mg. of pontocaine to 5 mg. of ephedrine and finally decided upon that of 1 mg. of pontocaine to 3 mg. of ephedrine, which appears to be quite as effective. This we secured by mixing 1 cc. of 1 per cent pontocaine, 0.6 cc. of 5 per cent ephedrine and 1.4 cc. of 10 per cent dextrose. This mixture thus contains 10 mg. of pontocaine and 30 mg. of ephedrine in 3 cc. of solution. The volume injected is dependent upon the desired dosage of pontocaine and is arrived at as in the original technique. It would be possible to draw into the syringe just the desired dosage of each of these drugs but there is less error in measuring the larger dosages and discarding the portion not needed.

In all cases the lumbar puncture and injection were made with the patient in the lateral position, the site of the puncture being either L2 or L3. The solution was injected at a little more than average rate, the injection taking from 4 to 6 seconds. No barbotage was employed to obtain the desired level. Immediately following the injection of the agent the patients were placed in the supine position, with a pillow under the head and shoulders and tilted to a 10 degree Trendelenburg position, which effectively pools the agent in the mid-thoracic region, since the anesthetic mixture is hyperbaric. Levels of anesthesia up to T4 or T5 are thus secured.

CLINICAL RESULTS

The patients were not selected, but were taken in consecutive order and chosen only because they were considered suitable for spinal anesthesia. They ranged in age from 18 to 82 years. There were 115 females and 52 males. The previously described technique of mixing and injection was employed in all cases. Our modification of decreasing the dosage of ephedrine was used whenever the selected dosage of pontocaine was more than 5 mg.

The maximum dose of 10 mg. pontocaine was administered to only eight patients, while 107 received 8 mg. (Table 1). In 125 instances the dose of ephedrine was approximately 25 mg. while the 50 mg. dose was given only three times. There were six cases in this series in which little or no analgesia was secured and in these results were classified as unsatisfactory. These failures we felt to be due to technical errors that reasonably may be expected in a teaching department. As is shown in Table 2, we found it necessary to supplement the spinal anesthetic in 47 patients because of pain. In 33 of these cases the supplementation was done before an elapsed time of one and one-half hours and the results should be considered as not wholly satisfactory. Some of these failures might legitimately be charged to the "trial and error" method by which we arrived at the optimum dosages. Twenty-eight patients received a

TABLE 1.—*Showing the various surgical procedures and the number of cases of each type. The actual number of patients receiving the various doses of pontocaine is also shown.*

Surgical Procedures	Dosage of Pontocaine Milligrams								
	3	4	5	6	7	8	9	10	Total
Pelvic Laparotomies			1	4		54		2	61
Vaginal Repair and Hysterectomy	1	1	4	2		8			16
Hernia Repair			5	5	4	18			32
Nephrectomy				2	1	4			7
Cholecystectomy				1		2		1	4
Cesarean			9	4		1			14
Exploratory and Appendectomy				2		8		2	12
Extremity		1	1			3			5
Laminectomy and Spinal Fusion						4		3	7
Suprapubic Bladder			1			4			5
Transurethral and Rectal Prolapse			1	1	1	1			4
Total	1	2	22	21	6	107		8	167

TABLE 2.—*Showing the duration of analgesia for various surgical procedures and the length of time between the start of operation and the need for supplement for pain.*

Surgical Procedures	Duration Analgesia Minutes					Onset of Pain Min. after start of Operation				
	0	30	60	90	120	0	15	30	60	90
Pelvic Laparotomies 2		4	9	24	22	2		4	9	8
Vaginal Repair and Hysterectomy ..		1	2	7	6				1	1
Hernia Repair 2		1	9	17	3	2		1	2	
Nephrectomy		3		4			1	2		
Cholecystectomy 1				2	1	1		1		
Cesarean		1	7	4	2			1	3	
Exploratory and Appendectomy 1		1	3	6	1	1	2		1	
Extremity			2	2	1					
Laminectomy and Spinal Fusion ..					7					
Suprapubic Bladder			1	3	1				2	
Transurethral and Rectal Prolapse			1	2	1				2	
Total 6		11	34	71	45	6	3	9	20	9

supplement of sodium pentobarbital or sodium pentothal intravenously to produce amnesia for the purpose of relieving nausea, apprehension or other of the unpleasant reactions sometimes observed in spinal analgesia.

Because of personnel shortages we found it impossible to check accurately the exact termination of the analgesia in many of those instances in which the anesthetic outlasted the surgical operation. In such cases we have considered the analgesia to have ended when the patient left the operating room. Actually, therefore, in those cases in which a supplement because of pain was not required, the effect of the anesthetic lasted an undetermined time longer than is indicated in Table 2. We were impressed with the fact that in the majority of cases effective analgesia lasted more than one and one-half hours, which compares favorably with that received from twice the dosage of pontocaine when ephedrine is omitted. If we may rightly assume that smaller doses of agent carry less hazard, then we must accept the conclusion that this technique will prove beneficial, for we are convinced that it is possible to secure satisfactory analgesia using these small doses in all types of operations in which a spinal anesthetic is commonly considered to be indicated.

An occasional delay in onset of analgesia has been noted and this may account for some of the cases in which results were listed as failures. However, one encounters a certain number of cases of delayed onset when using pontocaine and dextrose alone. In most instances satisfactory analgesia has been achieved by the time the patient is draped and ready for the surgeon to begin.

The incidence of severe hypotension is not significantly different than it is when only pontocaine and dextrose are used. In this series, 54 patients exhibited a variance of 40 or more mm. Hg. blood pressure, but only a few of these showed a severe drop initially. It was observed that this variation in blood pressure occurred in the course of prolonged operations, following excessive traction and handling of the abdominal viscera and other shock inducing procedures. Potter and Whitacre[6] observed that little or no generalized systemic vasoconstriction resulted from intrathecal injection of ephedrine. Our experience substantiates this observation, since it was found necessary to inject ephedrine subcutaneously or intravenously in order to maintain satisfactory blood pressure levels. The effect of such vasoconstrictor agents was that which might be expected from the dosage given and showed no tendency to be influenced by any amount that was administered intrathecally.

Headaches occurred in 10 patients of this series. In two they were very mild and transient and in three others they lasted from one to three days. One of the patients had a headache before the operation. Only three of the patients presented the typical symptoms of post spinal anesthesia headache, and in them the headache terminated spontaneously within a few days. Nausea and vomiting occurred 13 times in the operating room and was observed three times postoperatively. We do not feel that the intrathecal administration of ephedrine has materially altered the incidence of the commonly seen complications of spinal analgesia. There was no instance in which a serious untoward reaction occurred. There were no deaths in the series.

SUMMARY

The intrathecal injection of ephedrine has been found to potentiate the effect of pontocaine-dextrose to the extent that doses of 5 to 8 mg. of pontocaine produce the same degree and duration of analgesia that may be expected from 12 to 16 mg. of that agent without the addition of the vasoconstrictor. This technique has been found to be useful in all types of operations in which spinal analgesia is the method of choice, including intra-abdominal operations.

The addition of 3 mg. of ephedrine to each milligram of pontocaine appears to be quite as effective as the ratio of five to one previously reported by other investigators, and might be expected to carry less hazard of undesirable ischemia of the cord and nerve roots.

In a reported series of 167 cases no serious complication was encountered and the incidence of minor undesirable reactions did not appear to be increased by this procedure. It is felt that the results of this comparatively small series are sufficiently encouraging to warrant further investigation and trial.

Discussion by CHARLES F. MCCUSKEY, M.D., *Los Angeles*

Dr. Martinson and Dr. Leffingwell have presented an interesting discussion of the use of vasoconstrictors intrathecally. Prolongation of anesthesia, in conjunction with a reduction of the dose of spinal anesthetic agent, should increase the safety factor.

The use of hyperbaric solutions of pontocaine and dextrose for upper abdominal procedures, when the height of anes-

thesia is obtained by tilting the head of the table downward, carries the more concentrated anesthetic solution to the upper levels rapidly. The tendency toward respiratory complications is thus greater than when an isobaric solution is used. When a vasoconstrictor is added to the intrathecal agent the onset of anesthesia is usually slower and the length of time required for the anesthetic agent to become fixed is increased. Following the injection of pontocaine it is ordinarily considered safe to place the patient in Trendelenburg position after 15 minutes. When ephedrine or other vasoconstrictors are added, this time should be increased by 10 minutes.

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Inflammation as Considered by the Radiologist

Thomas M. Fullenlove, M.D., *San Francisco*

Celsus (25 B.C.-45 A.D.) first stated our classic definition of inflammation in the following terms "Notae vero inflammationis sunt quatuor, rubor et tumor, cum calore et dolore." (Truly the signs of inflammation are four, redness and swelling with heat and pain.)

Since then the theories of what was happening in the body and in the tissues of an inflammatory process have changed with the passing centuries. It is the intention of this paper to bring up to date our thinking of what actually happens in inflammation and to correlate the experimental work in the use of x-ray in inflammation.

Inflammation may be broadly defined as the complex vascular lymphatic and local tissue reaction elicited in higher animals by the presence of micro-organisms or of non-viable irritants.

What happens in inflammation?

1. *Increased fluid passage through the capillary endothelial wall.* This seems primarily due to: (a) elevation in capillary pressure and (b) increased capillary permeability. The first is most likely due to a local axon reflex affecting the capillaries and the second to the liberation by injured tissue of the permeability factor termed leukotoxine.

Over 50 years ago Cohnheim[3] called attention to the increased permeability of minute vessels in an inflamed area. This early concept has been fully substantiated by the use of various techniques such as are involved, for instance, in studying the local accumulation within injured areas of intravenously injected dyes or finely divided material. Following injection trypan blue accumulates in the inflamed areas, staining them and demonstrating capillary permeability.[14]

Menkin[15] has conclusively shown that besides histamine, another substance which he calls leukotoxine is released in an inflamed area and increases capillary permeability. He has isolated this substance and definitely proved it to be separate from histamine. Local nervous reflexes probably play a role in modifying the initial development of the inflammatory reaction.[16] A transient increase in capillary pressure following the application of an irritant was apparently referable to a local axon reflex.

Krogh[12] noted marked capillary dilatation of mucous membranes that extended for a considerable distance beyond the irritant. When the irritant was applied after section and degeneration of the nerves, the affected capillaries became partially dilated over a localized area.

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2. *Localization of the irritant.* The walling off of an inflamed area seems to be due to an enhanced passage of fibrinogen through the more permeable capillary wall. The draining lymphatics are blocked by thrombi and a fibrinous network. Various secondary factors such as presence of immune bodies in anaphylactic or allergic inflammation may reinforce the basic mechanism.

Menkin[20] has shown that *fixation* of powerfully necrotizing irritants such as Staphylococcus aureus occurs within two hours. Mild irritants, such as hemolytic streptococci, produce a delayed reaction, thus allowing relatively free penetration of the irritant into the circulation for a considerable period of time. Blockade of the draining lymphatics in such instances often takes place as late as two days following the introduction of the irritant.

3. *Migration of leukocytes.* The first cells to migrate into an inflamed area are polymorphonuclear leukocytes. This is related to the freeing of leukotoxine by the injured tissue. It contains factors concerned with both permeability and chemotaxis.

Menkin[17] has shown that leukotoxine is chemotactic both in the body and in the test tube.

The polymorphonuclear cells are gradually displaced by macrophages. The cell changes in acute inflammation seem to be conditioned by the pH of the exudate which in turn is often referable to disturbance in the local carbohydrate metabolism. The development of a local acidosis seems to injure the polymorphonuclear cells. Macrophages survive and predominate when the pH falls to the level of about 6.9 or 6.8. Further reduction in the pH kills all types of leukocytes and frank pus ensues.

Schade[28] reported that pus from acute abscesses had a pH ranging from 5.95 to 6.50; the pH of normal tissue fluid ranging from about pH 7.10 to pH 7.40. Menkin[18] injected turpentine in the pleural cavity and studied the pH and cellular response from day to day. As the inflammatory process progressed the pH changed from alkaline to acid. This usually occurred two to three days after injection of the irritant. Along with this decrease in pH there was a change in the differential leukocyte count. The percentage of polymorphonuclear cells fell, whereas the percentage of mononuclear phagocytes rose. The percentage of lymphocytes evidently plays no significant role in these cellular changes. The change in pH was shown to occur first. Menkin and Warner[21] showed that the pH was determined by the rate of lactic acid formation and the depletion of the alkali reserve at the site of injury.

With increase in the inflammatory reaction, there is a tendency for increased glycolytic activity as shown by a rise in lactic acid formation. This is ac-

companied by a fall in the CO_2 capacity, and the pH correspondingly drops. A true lactic acidosis results at the site of the inflammation. (See Chart 1.)

Effect of X-Ray on Normal Tissue.

Wolfenden and Ross,[32] Wyckoff,[33] and many others[23] have experimentally shown that radiation in huge quantities (tens of thousands of roentgens) is bactericidal. These doses would produce untold damage if used on living human tissues.

Normal cells have a specific range of sensitiveness.[6] By "specific range of sensitiveness" is meant that, when exposed to the same dose of rays under the same conditions, some kinds of cells are influenced more rapidly and to a greater degree than other kinds. At any particular time, however, all cells of one kind are not affected to the same degree by the same dose of rays. This is because the sensitiveness of different cells varies according to the phase of metabolism in which they happen to be at the time of irradiation. Cells that are actively dividing are more sensitive than those in the resting phase. Any factor which increases the rate of mitosis tends to increase the radiosensitiveness of the cells. The sensitivity of different kinds of cells is closely related to their degree of differentiation and to their life cycle.

The susceptibility of cells to radiation in order is as follows: (1) Lymphoid cells (lymphocytes in spleen, lymph nodes, intestinal lymph follicles, circulating blood, bone marrow, thymus, tonsil and other structures where these cells are present); (2) polymorphonuclear leukocytes in blood or tissue; (3) Epithelial cells (a) basal epithelium of certain secretory glands especially salivary; (b) basal epithelium (spermatogonial cells) of testis and follicular epithelium of ovary; (c) basal epithelium of skin, mucous membrane and certain organs such as the stomach and small intestines; (d) alveolar epithelium of lungs and of bile ducts; (e) epithelium of kidney tubules; (4) Endothelial cells of blood vessels, pleura and peritoneum; (5) Connective tissue cells; (6) Muscle cells; (7) Bone cells; (8) Fat cells; (9) Nerve cells.

Other Responses:

1. Vasodilatation occurs in tissue that has been irradiated with small doses of x-ray which begins in about six hours and lasts 24 to 48 hours. The effect

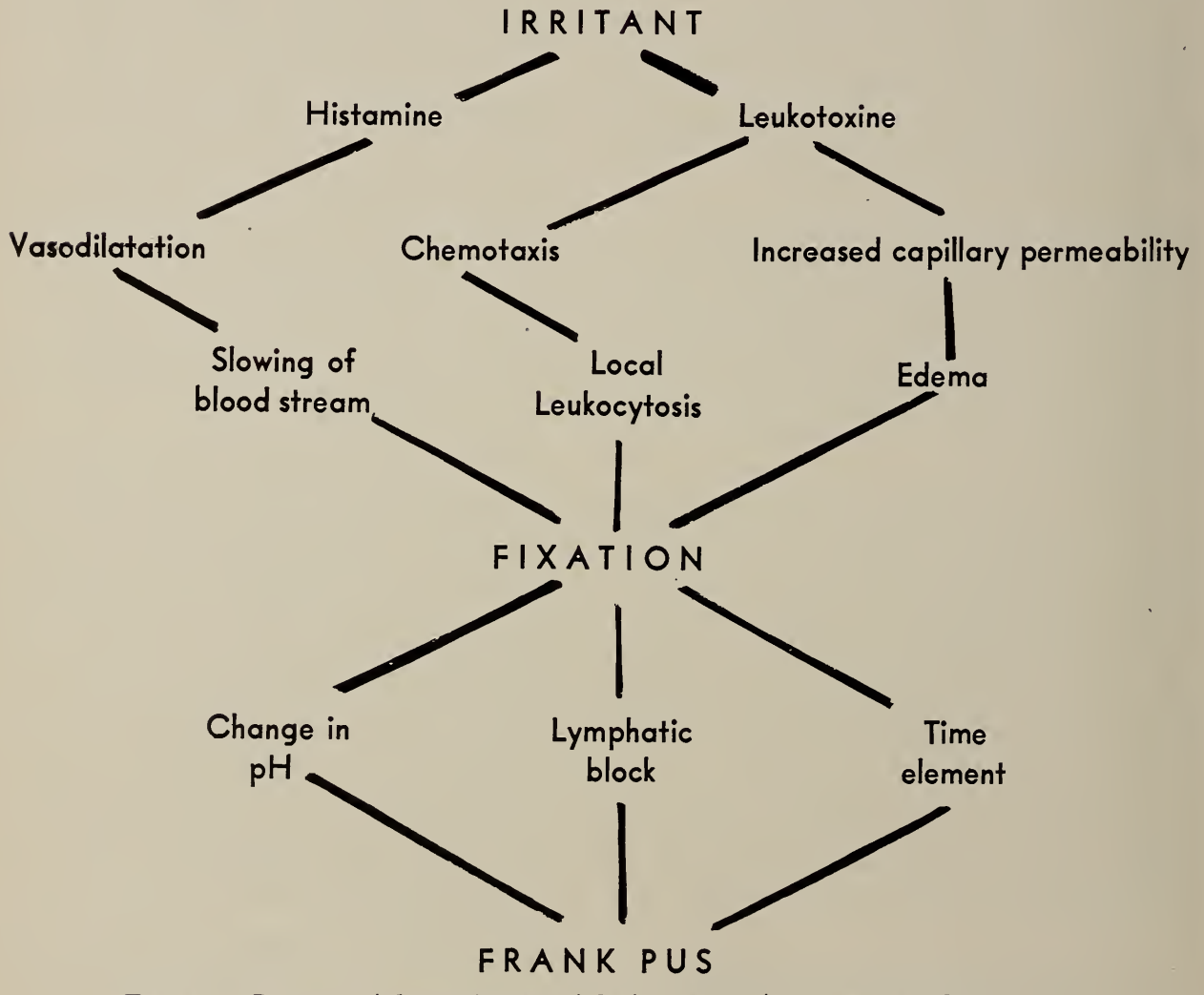


TABLE 1.—*Diagram of the mechanism of the formation of pus in acute inflammation.*

is more prompt with low voltage than with hard radiation. At no time have thrombi occurred such as Menkin describes in inflammations during fixation. The process has indicated an increase in the rate and quantity of blood flow through the irradiated area of the type seen in active hyperemia. Pendergrass, Hodes and Griffith[24] tested 84 subjects on the extensor surface of the forearm. A capillary count was done at 9 a.m. after injection of 1-1000 histamine, with further counts done at 4 p.m. and the next morning at 9 o'clock. The main factors used were 200 KV. ½ cu plus 1 al. filter. At 15 cm. distance 333 r were given in ¾ minutes. A significant dilating effect on the skin capillaries was observed after six hours. This was largely gone after 24 hours. At 50 cm. distance, 301 r were given in 7.2 minutes. A distinct dilating effect was observed in 6 hours. This was still present after 24 hours. At 50 cm. distance, 308 r were given in 30.8 minutes. No significant change was seen in the skin capillaries in 6 hours and no definite effect was noticed in 24 hours. At 3 cm. distance 50 KV. was used and 300 r were given in one minute. A moderate capillary dilatation was noticed in six hours. This was increased and more marked in 24 hours.

2. Vohra[31] showed irradiation produces a change in the pH concentration of the cell plasma accompanied by increased permeability of the cell membrane. Other changes are decrease in cell respiration and increase of glycolysis. Inhibition of mitosis, production of mutations and death of rapidly dividing cells are, according to Vohra, the three main effects of small doses of radiation.

3. Tchaperoff[30] reports the inactivation of paraaminobenzoic acid by 50 r at 190 KV. This substance is important as a bacterial growth factor and is released by the tissues or synthesized in infections.

How X-Rays Affect Inflammation.

A. Active hyperemia in capillaries is induced by x-rays.[24]

B. The destruction of polymorphonuclear cells and lymphocytes releases proteolytic enzymes which dissolve dead tissue.[22] The lymph and blood channels are cleared of debris by the dual action of the radiation and the enzymes.

C. By changing the permeability, the hydrogen ion concentration and the carbohydrate metabolism of the injured cell and the surrounding cell plasma.[31]

D. By increasing the phagocytic ability of polymorphonuclear leukocytes and producing a generalized physicochemical change in the plasma which is antitoxic in nature. Crane[5] in 1907 showed that an increase in the opsonic index followed irradiation of infections. Hektoen [10,11] and other investigators[4] confirmed this. Glenn[8] showed the marked increase of phagocytic index against Staphylococcus aureus in rabbits produced 48 to 96 hours after irradiation with 100 r in air using 140 KV. Rosselet and Sarian[26,27] demonstrated this increased phagocytic activity by separating cells and plasma of irradiated blood. Irradiated leukocytes were then mixed with non-irradiated plasma and non-irradiated leukocytes with irradiated plasma and tested for phagocytic power, using suspensions containing Staphylococcus. With the first mixture (i.e. irradiated leukocytes and non-irradiated plasma) no increase in phagocytic activity was noted, but with the non-irradiated leukocytes and irradiated plasma phagocytosis was definitely increased. They concluded that the result was due to some physicochemical change in the plasma. Bisgard, Hunt, Neely and Scott[1] definitely demonstrated an antitoxic factor present in the blood stream of rabbits 48 hours after irradiation of the abdomen. This substance, while not isolated, gave a 60 per cent survival rate to inoculated rabbits while all controls died. When the peritoneal washings of rabbits so treated were injected into the peritoneal cavity of stock rabbits, all survived while the controls died.

E. By destroying young fibroblasts. This occurs when larger total dosages are used and is more important in chronic inflammation and in scar formation. Doljanski, Goldhaber and Halberstaedter[7] showed that the immediate lethal dose of x-rays for rat sarcoma is the same as that for normal rat fibroblasts.

* * *

In the past 50 years practically all known inflammatory conditions have been treated with x-rays. Even before we knew the reason why, the beneficial effect in inflammatory processes was clinically demonstrated. The empirical use of x-rays in inflammation has been amply justified by both clinical and experimental studies over the years. In spite of the fact that x-ray therapy is non-specific and beneficial to all types of inflammation, if given in the proper dosage, the stage of development of the inflammation is very important. If irradiation in proper amounts is given before fixation (as described by Menkin), resolution will occur, if given after, pus formation is enhanced. The state of well-being of the body is very essential. In a debilitated individual, the response is much less than in a healthy organism.

The stage of an inflammatory process can be divided into acute, subacute and chronic for clinical purposes. Perhaps the acute and subacute stages would be divided by the occurrence of fixation in the tissues. The chronic stage most likely would be measured by the presence of fibroblast and lymphocytic infiltration.

CONCLUSION

Experimental evidence of how an inflammation occurs is presented. The experimental data of the effect of x-ray on an inflammatory process shows that: (1) An active hyperemia is produced; (2) White blood cells are destroyed; (3) The permeability, pH and carbohydrate and metabolism of the cell and plasma are changed; (4) Phagocytosis is increased and an antitoxic factor is formed in the plasma; (5) Fibroblasts are destroyed.

450 Sutter Street.

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Laboratory Procedures in Diagnosis of Brucellosis

Albert G. Bower, M.D., and Jack S. Chudnoff, M.D., *Los Angeles*

EXCEPT for a positive culture of the infecting Brucella organism obtained from a suspected patient, there is no single completely reliable and satisfactory diagnostic procedure for brucellosis. However, since the disease is so bizarre and protean in its manifestations; since culturing the organism is rarely accomplished by the practitioner due to technical difficulties and to its slow growth; and since some reliable workers[10] estimate that less than 10 per cent of chronic brucellosis cases have an abrupt initial febrile onset such as occurs dramatically in the recognizable acute types of the disease, the diagnosis of brucellosis is based almost invariably upon laboratory procedures. The disease, furthermore, stands almost alone in the unanimity with which the above statement is supported by the medical profession, and in the knowledge than there are no pathognomonic findings in the chronic forms of human brucellosis.

When aliquot parts of the same patient's serum have been apportioned to 15 different laboratories of average standing, it has been common to secure 15 different results, varying from negative on the one extreme to positive in final dilutions as widely divergent as 1:40 to 1:1200.[3] There are many reasons for such variances, among which are unsuitable or isoagglutinating antigens and the recently demonstrated presence of "blocking antibodies" similar in mechanism to those described in Rh factor work.[6]

The identical techniques applied by Weiner and Race in their original work have revealed the masking effect of saline-suspended antigens, the phenomenon of dissociation of the blocking systems by serial dilutions (thus uncovering an "inhibiting zone" titer), the effect of heat on freshly drawn serums in potentiating agglutinations, and the enhancement of agglutinations by substitution of albumin for saline in antigen suspensions.

Neither bacteriologic antigens nor bacteriologic methods are universally standardized. It is suggested that if suitably located central testing laboratories were set up throughout the state with the cooperation of the various local health facilities and with the State Department of Public Health, these serious deficiencies might be largely corrected: (1) by using smooth-type sub-cultures under 48 hours old for antigenic material; (2) by testing at the same time against bovine, porcine, and caprine strains; and (3) by uniformly standardizing bacteriologic methods and materials, old and new. At these stations, special provisions for studies of brucella cultures might also be made. Adequately handled blood cultures repeatedly have been positive, not only in acute cases, but *also in afebrile chronic cases of many months' duration*, a fact not generally known.

What constitutes a positive agglutination as conducted under the usual present conditions? No given numerical value: the widely held opinion that a positive agglutination titer of 1:80 is diagnostic is erroneous. Much more significant is a changing titer, repeated examination of the blood from the same individual at two-week intervals showing a titer which either rises or falls during the period of observation and is positive in a dilution of 1:80 or higher. Huddleston[7] reports 29 per cent of negative agglutinations in 100 bacteriologically proven cases due to *Br. abortus*. Dooley,[2] on the other hand, in 1932 studied 263 boys known to be ingesting raw milk from an infected herd which was concurrently responsible for two known clinical cases. They showed no manifestations of the disease whatever, yet 41 per cent of these boys had agglutination titers ranging from 1:40 to 1:1200 for brucella and 15 of these boys over prolonged periods of observation maintained titers of 1:320 and higher, but were asymptomatic.

Although this is not widely known, 90 per cent of service men vaccinated against cholera in the past war gave positive brucella agglutinations in titers as high as 1:1640.[4] Also, the opsonic index became strongly positive. Similarly, in approximately 11 per cent of cases, tularemia may give rise to false agglutinations for brucellosis.

Complement fixation has not been utilized to any degree in the laboratory diagnosis of brucellosis because it does not seem to be of value.[8] It has been attempted repeatedly in the study of animal brucellosis where no agglutination titers are present but where the disease is suspected. It is not technically as easy to perform as agglutination and repeated ambiguous results have been ascribed to theoretic anti-complement, to poor antibody formation, etc. As it appears to offer no advantage to the laboratory, its use has been circumscribed.

Reliance upon a positive skin test alone as diagnostic of existing active brucellosis is entirely erroneous.[11] Negative brucella skin tests in the presence of bacteremia have been reported frequently,[9] and, conversely, large numbers of people without clinical manifestations have been shown to have positive skin tests.

The danger of local tissue sloughing should be remembered when skin testing is done routinely and with large doses. Repeated skin testing with the vaccines commonly employed sometimes (but not invariably) causes significant agglutination titers to develop. Thus the effect of intradermal vaccines, used either as diagnostic tests or for therapeutic desensitization, may invalidate future aid from the laboratory.[5] This is more common than usually believed. It is

From the services of the Los Angeles County Hospital, Communicable Disease Division, and the Los Angeles County Health Department.

apparent that intradermal tests as at present widely used in diagnosis are of dubious value and widely abused in interpretation.

There exists in medical literature a philosophy that "brucella sensitization" may be a clinical entity.[1] Impressive data has been accumulated and interpreted in a manner which would tend significantly to correlate positive intradermal tests with psychoneurosis, allergy, and chronic arthritis. Such trends are to be evaluated with caution and deliberation, as they have appeared before in conjunction with other intradermal tests such as the tuberculin and coccidiomycin reactions. Undoubtedly, brucella sensitized individuals will be re-examined in the future with new diagnostic techniques and therapeutic methods, and it is probable that an accurate evaluation will clarify the issue. It is yet to be proven that the skin test is of greater significance relative to brucellosis than is the tuberculin skin test in relation to tuberculosis.

Similarly, the presence or absence of opsonophagocytic phenomena merely indicates: either (1) the presence of operative immunity (inasmuch as the phagocytes are seen to ingest living virulent organisms), or (2) a non-infected susceptible status (inasmuch as no phagocytosis occurs due to lack of the development of opsonins to stimulate ingestion of brucella organisms by the neutrophiles). Furthermore, the test is technically exacting and unless performed by well-qualified bacteriologists is seldom of any value. In any event, it does not prove active disease either present or absent.

From this discussion, it is apparent that aside from obtaining a positive culture of the organism, the diagnosis of brucellosis depends upon:

1. Evaluation of the epidemiological data when available.
2. Evaluation of clinical signs and symptoms.
3. Laboratory procedures comprehensive in scope, universally standardized, frequently repeated, technically dependable, and considered both in relationship to each other and to the clinical picture. Imperfect and unsatisfactory as laboratory tests appear to be at present, when properly evaluated they are the strongest available links in the chain of evidence leading to an acceptable diagnosis of human brucellosis.

The frontiers in medicine, both diagnostic and therapeutic, are continuously expanding. Diagnostically, the revelation of the blocking-antibody phenomena may add much to the clarification or substantiation of difficult diagnoses. It has been recently demonstrated that egg-yolk embryo inoculations will support the growth of brucella organisms [13] and that this technique allows also for an *in vitro* test of the chemo-sensitivity of the organism recovered or cultured. Utilizing this technique, therapeutically, it has been demonstrated that the combination of streptomycin and sulfa drugs in adequate dosage provides a more consistently potent antidote to brucellosis than has hitherto been known. In the not infrequent instances where the last clinical resort of the physician is a "therapeutic trial" to combat the malady, this therapeutic combination may well confirm in restrospect a clinical diagnosis supported previously on the gossamer of controversial data.

The need for attempting to standardize and improve existing facilities for the diagnosis of brucellosis—a need that is urgent in view of the constantly increasing number of cases reported—is pointed out.

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Influence of Mercurial Diuretics on the Excretion of Sodium, Potassium and Chlorides

Donald E. Griggs, M.D., and Varner J. Johns, M.D., *Los Angeles*

IT has been shown repeatedly that both mercurial diuretics and low sodium diets cause diuresis in patients with congestive heart failure, providing there is an adequate fluid intake. Most patients find a low sodium diet most unpalatable and many would prefer an occasional injection of a mercurial diuretic with less extreme sodium reduction in the diet. This study was undertaken to determine if possible the exact value of mercurial diuretics in augmenting or partially replacing the unpalatable extremely low sodium diets which have recently been used as an effective diuretic measure.

METHOD OF STUDY

This is a report based upon the study of ten patients, nine of whom had congestive heart failure, and one of whom had portal cirrhosis. They were maintained on digitalis and were given no aminophyllin. Ammonium chloride was used in Cases Nos. 1, 3 and 9. All patients were maintained on a daily fluid intake of 3,000 cc. They were given diets containing one gram of sodium chloride daily except for Case No. 6 where the sodium chloride was raised during the course of the study to determine the effect of this increase in sodium intake upon its excretion. Urinary output was measured from 8:00 a.m. to 8:00 a.m. Two cc. (one cc. in Case No. 7) of a mercurial diuretic (mercuhydrin) was administered intravenously every third or fourth day. This was given at the beginning of the 24-hour period so that on the day of injection the mineral excretion was measured for the following 24-hour period.

Determinations of sodium and potassium were made by means of a flame photometer. This apparatus is similar to that described by Barnes et al[1] but the Beckman Spectrophotometer was used as a monochromator and light measuring instrument. Satisfactory concentrations were obtained by diluting the urine 1 to 50 with distilled water. The calibration was made by using standard sodium and potassium solutions containing 5 to 50 parts per million.

Chloride determinations were performed by direct potentiometric titration with silver nitrate using a National Tech. Lab. pH meter with silver and glass electrodes.

These determinations were done by Albert L. Chaney, Ph.D.

REPORT OF CASES

Case No. 1.—(Figure 1.) The patient received ammonium chloride 4 gm. per day during the entire period of observation. On the first three days he was digitalized and thereafter received only maintenance doses of digitalis. On the day before the first mercuhydrin injection was given, the total sodium excretion was greater than at any subsequent time. This was probably due to the fact that the patient was being digitalized at that time. Thereafter the total sodium excretion was greater in the 24-hour urine specimen after injection of the diuretic than on any of the other 24-hour urine specimens.

The percentage of sodium excretion or grams per liter was also increased in the 24-hour urine specimens following the mercurial diuretic.

Case No. 2.—The patient was digitalized prior to hospital entry. When he entered the hospital there was evidence of digitalis intoxication with anorexia, nausea, vomiting and multiple ventricular premature contractions. These disappeared after six days, and digitalis therapy was resumed. Following the resumption of digitalis on the sixth day there was again noted an increase of total sodium excretion. Along with this increase of sodium excretion there was a corresponding increase of both the percentage and the total chloride excretion. With each injection there was a decrease of the percentage of potassium excretion, but due to the increased urinary output there was no corresponding decrease in the total potassium excreted.

Case No. 3.—This patient received on the first day 1.2 mg. of digitoxin with no observed effect on the mineral excretion. The findings were essentially the same as in Case No. 2. On the days of the mercurial injection the percentages of sodium and chloride excretion were increased while the potassium excretion was decreased.

Case No. 4.—This patient was on maintenance doses of digitalis before and during the study. The sodium and chloride excretion was increased on the days the mercurial was used. This was more marked with the first injection. As the patient depleted his reserves of body sodium by an output of sodium which exceeded the 1 gm. daily sodium chloride intake the total excretion of sodium became progressively lower. In spite of this the percentage of sodium and chloride continued to be higher on the days the diuretic was administered.

The output was not recorded on the last day that mercuhydrin was injected so we were unable to determine the total sodium output for that day.

Case No. 5.—This patient was on maintenance doses of digitalis during the entire study, as he had been previously digitalized.

There was an increase in both the percentage and total excretion of sodium and chloride on the days of mercuhydrin injection but unlike the previous cases no material change in the potassium excretion was observed.

Case No. 6.—(Figure 2.) This patient was on digitoxin 0.2 mg. daily during the entire study. Regardless of urinary output there was an increase in the percentage of sodium and chloride excretion on the days of mercuhydrin administration. The values for potassium were inconstant though

From the Department of Internal Medicine of the College of Medical Evangelists. This study was aided by a grant from the Lakeside Laboratories.

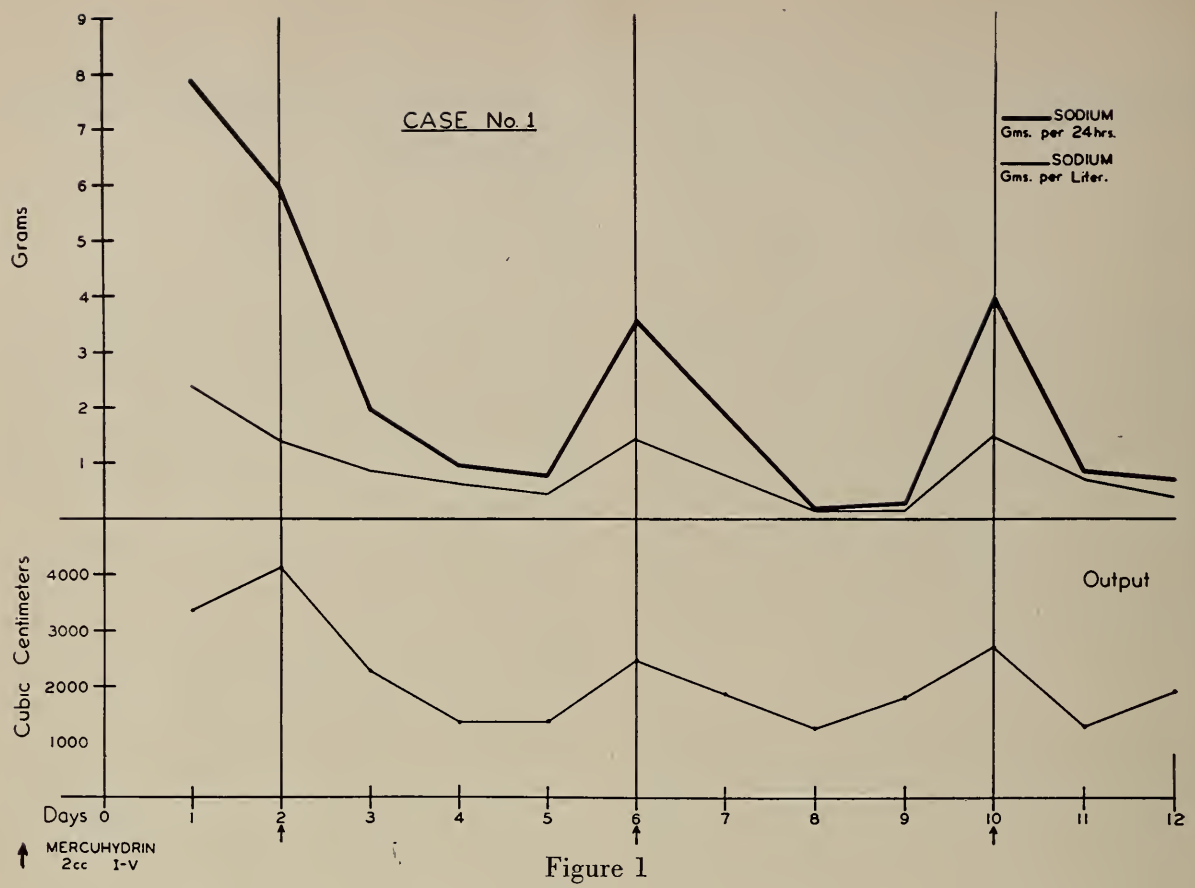


Figure 1

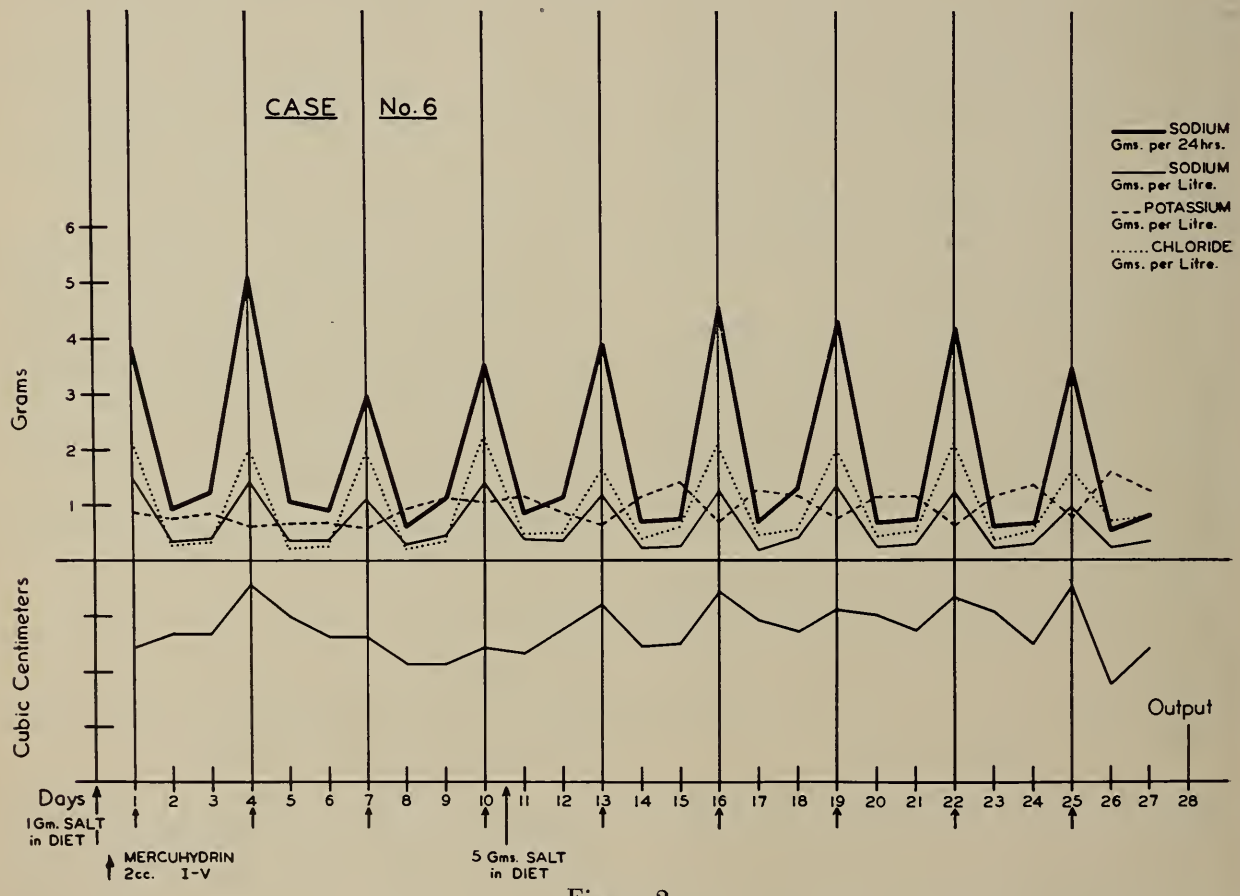


Figure 2

they tended to be lower on the days of the injection. On the eleventh day the sodium chloride intake was increased from 1 gm. to 5 gm. with no significant change in urinary output of sodium. In spite of the increase of sodium chloride intake he had no recurrence of signs or symptoms of congestive failure. This may be due to the fact that the sodium chloride excretion with the diuretics practically equalled this 5 gm. intake.

This patient had three thoracenteses, done on the first, tenth, and eighteenth days of our study. A total of 3,350 cc. of pleural fluid was removed. Only two specimens were analyzed for the sodium content of the pleural fluid. The first contained 2.85 gm. per liter and the second 4.5 gm. per liter. The pleural fluid had a higher sodium content than the average percentage in the urine so that this seems to be an important method of removing sodium from the body.

Case No. 7.—(Figure 3.) This patient was digitalized with digitoxin during the first two days of our study. As with all the other cases more sodium was excreted on the days of mercurial injection than on the other days. The percentage of sodium was also greater. This case demonstrates the fact that as the sodium in the body is depleted the sodium excretion becomes progressively lower. This case also shows the amount of sodium excreted on six successive days without mercurial diuretics. In this patient only 1 cc. of mercuhydrin was administered every third day. While the urinary output in this patient was not large the total and percentage sodium excretion was almost as great as in the other patients who were given 2 cc. injections of mercuhydrin.

Case No. 8.—This patient received ammonium chloride 4 gm. daily during the entire study. He was digitalized during the first three days of the study. The high sodium excretion on the second day may in part be due to the digitalis. This case demonstrates again the decrease in sodium excretion as the sodium in the body is depleted by an excretion exceeding the 1 gm. daily sodium chloride intake.

Case No. 9.—This patient was on maintenance doses of digitoxin. Ammonium chloride 4 gm. daily was given during the entire study. Following the first two mercurial injections the sodium excretion, both the percentage and the total, was greater than at any other time. This was not true of the third injection.

Case No. 10.—This patient had portal cirrhosis with no evidence of congestive failure. The albumin globulin ratio was 3.6:3.0 gm. The 5 mg. bromsulphalein test showed a retention of 60 per cent after one-half hour and 35 per cent after one hour. The intravenous hippuric acid test showed an excretion of 0.16 gm. of benzoic acid in one hour. The non-protein nitrogen was 45. No digitalis or ammonium chloride was given. The sodium excretion was greater following the mercurial injections than at any other time. The total daily sodium excretion never exceeded 1 gm. even on the days the diuretic was given. The reason for this is not clear. This case is not included in the averages of the cases.

DISCUSSION

The average of the nine cases showed a sodium output of 0.81 gm. per liter on the days without the diuretic (Figure 4) and 1.96 gm. per liter on the days mercuhydrin was injected. The average total 24-hour output of sodium was 1.09 gm. on the days without injection and 4.83 gm. on the days of injection. This shows that the concentration of sodium in the urine was increased nearly two and one-half times

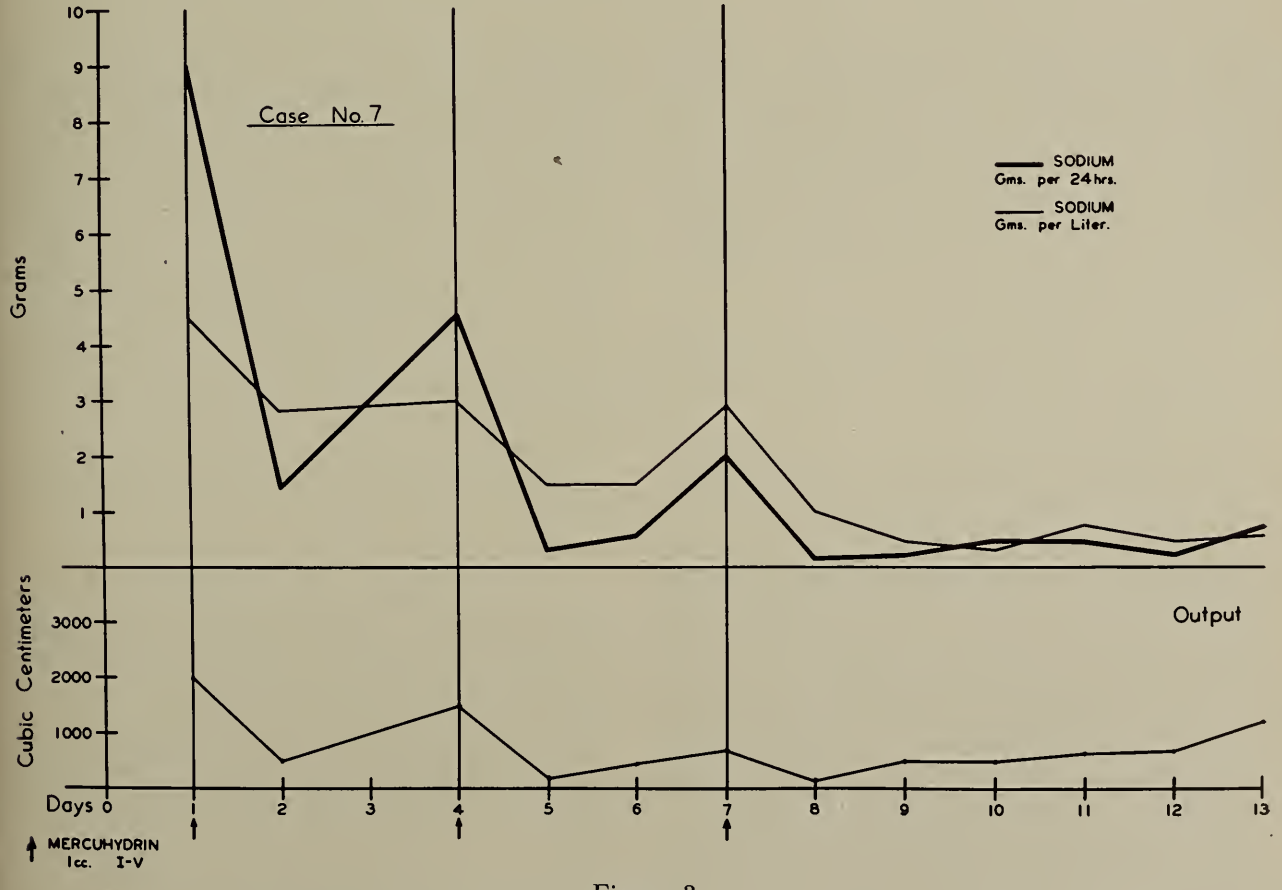


Figure 3

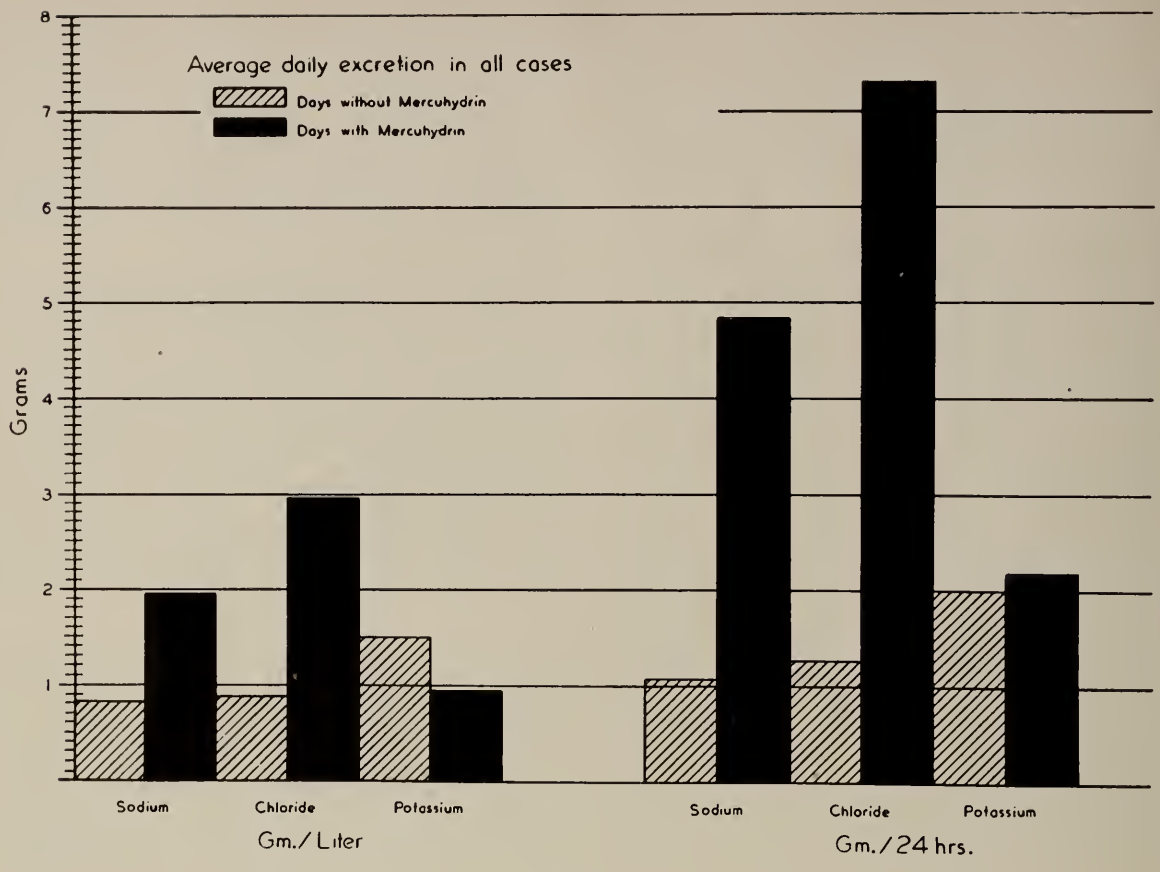


Figure 4

by the injection of the mercurial diuretic, while the average total excretion of sodium in 24 hours was increased more than four times by mercuhydrin injections. Reaser and Burch,[5] in an independent study, recently also found a marked increase both in the total and percentage sodium excretion after injections of a mercurial diuretic in a patient with congestive heart failure. They used a radioactive tracer Na^{22} to determine sodium excretion.

One gram of sodium (as we have measured it in the urine) is the equivalent of 2.54 gm. of sodium chloride which is the form in which dietary sodium is usually measured.

The average 24-hour excretion of 1.09 gm. of sodium on the days without injection is equivalent to 2.77 gm. of sodium chloride.

The average excretion of the 4.83 gm. of sodium for the 24 hours following the injection of mercuhydrin is equivalent to 12.27 gm. of sodium chloride or an increase of 9.5 gm. over the days the diuretic was not given. It would appear therefore from this small series that it may be possible by giving two injections of a mercurial diuretic weekly to increase the sodium chloride intake by 2.7 gm. per day. This would enable the patient to have a much more palatable diet without increasing sodium retention.

There was an actual decrease in the average percentage of potassium excreted in the urine following the injection of the mercurial diuretic. The average potassium in grams per liter decreased from 1.51 to 0.9 following the injections. Due, however, to the diuresis on the days of mercurial injection the total excretion of potassium was slightly greater on those days—2.16 gm. in 24 hours as compared with 2.01 gm. in 24 hours. Melville and Stehle[4] also found that the potassium excretion following the injection of mercurial diuretics is less than the sodium excretion.

The average percentage chloride excretion following an injection of the mercurial diuretic increased more than three and one-half times, from 0.83 to 2.94 gm. per liter. The average total 24-hour excretion of chlorides increased sixfold, from 1.17 to 7.3 gm.

This increased urinary concentration of chlorides was noted by Hatzieganu, Gavrila and Borbil,[3] and Bouyoucos[2] and Stockton.[6]

SUMMARY AND CONCLUSION

1. In a study of nine patients with congestive heart failure who were maintained on a low sodium diet, the injection of 2 cc. of a mercurial diuretic, mercuhydrin, caused the following changes in the urine during the 24 hours after its injection:

(a) The average concentration of sodium in the urine was increased nearly two and a half times. The total sodium excretion was increased more than four times.

(b) The average concentration of potassium in the urine was decreased 40 per cent, although due

to the diuresis there was a slight increase in the total excretion of potassium.

(c) The average chloride concentration in the urine was increased more than three and a half times. The total chloride excretion was increased six times.

2. The average total sodium excretion after the administration of 2 cc. mercuhydrin was 4.81 gm. This is the equivalent of 12.3 gm. of sodium chloride, which is the form in which dietary sodium is usually measured. This is an increased excretion of 9.5 gm. of sodium chloride over the days on which the mercurial diuretic was not given.

3. It appears possible that for brief periods at least, the injection of mercurial diuretics will permit a more palatable, higher sodium chloride diet without any increase in sodium retention.

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CASE REPORTS

◀ Parathyroid Carcinoma Causing Hyperparathyroidism
◀ Severe Stomatitis Due to Erythema Multiforme—Its Differentiation from Human Foot and Mouth Disease

Parathyroid Carcinoma Causing Hyperparathyroidism

JUSTIN R. DORGELOH, M.D., *Oakland*

IN a review of the 322 cases of parathyroid adenoma reported up to 1945 it is stated that multiple tumors were described in 20 instances.[2] The reviewers point out, however, that only two of the 20 cases were reported after 1938, the year in which Albright's paper on secondary hyperplasia of the parathyroids appeared. Hence, it would appear that multiple true adenomas of the parathyroids are rare.

Malignant adenomas of the parathyroids *causing hyperparathyroidism* are considered very rare by most authors. Alexander[1] and his coworkers were able to find only seven reports of such cases in their review. These reviewers, however, appended reports of 14 new cases of hyperparathyroidism, with the opinion that the adenoma in 13 of the cases was malignant. Criteria of malignancy were invasion of capsule or blood vessels, or, in some cases, merely certain cytologic features. Metastasis was not demonstrated in any of the 13 cases, and in the seven reviewed reports metastasis was described in only one instance. It would seem that classification of parathyroid tumors as benign or malignant has depended largely on debatable criteria of malignancy.

REPORT OF CASE

The patient, a 51-year-old Caucasian female, was first seen at St. Luke's Hospital in December, 1945. For two years she had experienced pain on movement of various joints. During the past year she had become very weak and had lost 24 pounds of weight. Vomiting had occurred during the last three months. Polyuria had been present for an unknown period of time. Incidental to an unrelated episode, asymptomatic calculi were demonstrated in the region of each kidney by roentgen examination in 1927.

Physical examination revealed a weak, ill woman with flaccid muscles. A mass was palpable in the region of the right lobe of the thyroid. The blood pressure was 142 mm. systolic and 82 mm. diastolic.

Laboratory studies demonstrated 10 gm. of hemoglobin per 100 cc. of blood, 3.8 million erythrocytes and 8,800 leukocytes per cubic mm. (the differential count of leukocytes was normal). The urine exhibited a specific gravity of 1.005. It contained 100 mg. of protein per 100 cc., and a large amount of calcium was demonstrated by the Sulkowitch test. Bence-Jones protein was not present. Microscopic examination revealed a few leukocytes and an occasional granular cast. Serum calcium was 18.5 mg., phosphorus 5.0 mg. per 100 cc. Alkaline phosphatase was 17.8 Bodansky units, acid phosphatase 1.5 units. Albumin was 3.4 gm., globulin 2.7 gm. per 100 cc. of serum. The non-protein nitrogen content was 54 mg. per 100 cc. of blood.

X-ray examination revealed generalized osteoporosis. In addition, there were cystic areas in ribs, cranium, vertebrae and long bones; some cystic lesions were apparently expansile. A rib fracture was demonstrated, as well as collapse of a vertebral body. Small calculi were seen in the region of each kidney. Diffuse renal calcification was not demonstrable.

Sternal puncture and rib biopsy were carried out. Exploration of the neck was performed Dec. 31, 1945. Two tumors were found. The smaller was encapsulated and located a few millimeters from the inferior border of the right lobe of the thyroid, from which the tumor was distinct. The larger tumor was incorporated within the right lobe of the thyroid, and was thought to be a thyroid adenoma until rapid microscopic examination revealed its nature. Both tumors were extirpated.

On the day following operation the blood calcium had dropped to 11.0 mg. per 100 cc. of serum. On Jan. 3 the calcium level was 9.0 mg., numbness of the mouth developed, and Chvostek's sign could be elicited. Despite continuous calcium therapy, the blood calcium dropped to as low as 7.3 mg. The level then quickly became and remained normal. Postoperative Sulkowitch tests of the urine revealed no abnormal amount of calcium.

The patient then returned to her family physician in another city, where she improved and x-rays demonstrated complete healing of bone lesions. She returned to St. Luke's Hospital Feb. 18, 1947, because of recurrence of former symptoms. The calcium level was found to be 13.3 mg. per 100 cc. of serum, phosphorus 2.3 mg. Roentgen examination revealed demineralization of the calvarium, without cystic areas. The ribs appeared normal, a new cystic lesion of a tibia had appeared, and the renal calculi were still present. Studies were interrupted by departure of the patient for treatment elsewhere.

TISSUE EXAMINATION

The rib biopsy specimen consisted of a little reddish tissue exhibiting no evidence of brownish color to gross examination. Microscopically, the typical picture of giant cell tumor was presented. Very little hemosiderin was apparent. The sternal puncture films contained very few cells other than non-nucleated erythrocytes. A few cells were relatively plump spindle-shaped forms with a vesicular, elongated nucleus. These conformed to the spindle cells found in sections of the giant cell tumor from the rib.

The smaller parathyroid tumor was 15x18x8 mm. in size. The smooth surface was completely encapsulated, and the bulging cut surface revealed a soft, tan, homogeneous tissue. The larger mass was 28x26x18 mm. in size, and was encapsulated except over a small area where it had been fused to a little thyroid tissue. Sections revealed a pinkish-gray tissue traversed by narrow and broad bands of firm white tissue.

Microscopically, the two tumors were similar. They were undoubtedly of parathyroid origin. There were masses and anastomosing columns of large polygonal and columnar cells (see Figures 1 and 2). Most of the cells were of the "chief cell" variety, with foamy cytoplasm. A moderate number were of "water clear" type, and a few oxyphil cells were present. The cells were much larger than normal, and many presented a very large nucleus with one or two very prominent nucleoli. An occasional mitotic figure was seen. The stroma was scant, save for areas of fibrosis in the larger tumor. The

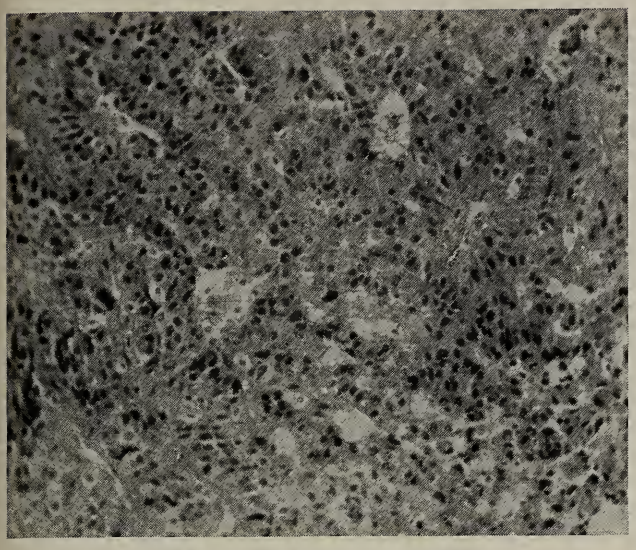


Figure 1.—Magnified 130 times.

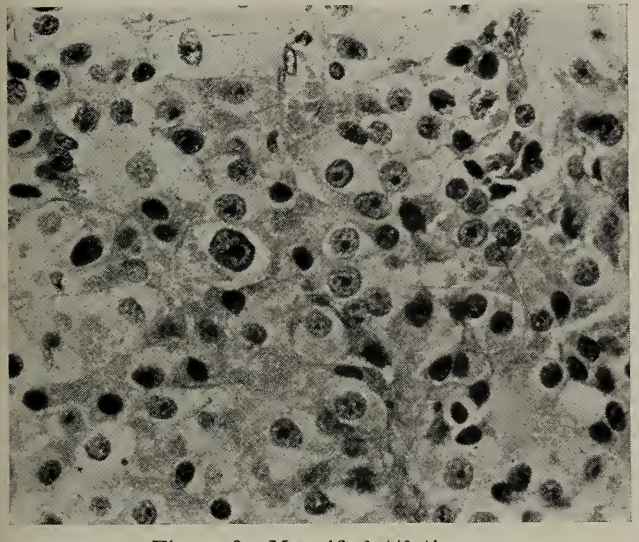


Figure 2.—Magnified 440 times.

latter tumor presented invasion of thyroid tissue and growth into the lumen of venules (see Figure 3). A small separate fragment of tissue removed during the surgical operation consisted of apparently normal thymic tissue enclosing a small amount of parathyroid tissue; the latter appeared normal.

ANIMAL INOCULATION

Extracts* of each tumor were injected intravenously into rabbits. The calcium level of each animal rose to an average value of 19 mg. per 100 cc. of serum, from a pre-injection level of 12 mg. The experiment was controlled by injection of other rabbits with various tissues.

DISCUSSION

The histologic features of the parathyroid tumors in the case reported were those commonly accepted as being indicative of malignancy. In view, however, of the fact that only one case of metastasis from a malignant adenoma of the parathyroid *with hyperparathyroidism* has been reported, a circumspect attitude in the diagnosis of "malignancy" would seem desirable. One might consider, in the present case, that the tumors represent multicentric origin or, on the other hand, malignant extension. According to either interpretation, this case presents a rare situation. Investigation of the recurrence of hyperparathyroidism in the patient was aborted by her decision to seek treatment elsewhere. A preliminary part of the investigation was to have been biopsy of the new tibial lesion to determine if it represented metastasis of parathyroid tissue, or merely another giant cell tumor.

*Method of Collip, as described in Physiol. Basis of Med. Pract., Best & Taylor, 3rd ed., p. 1185.

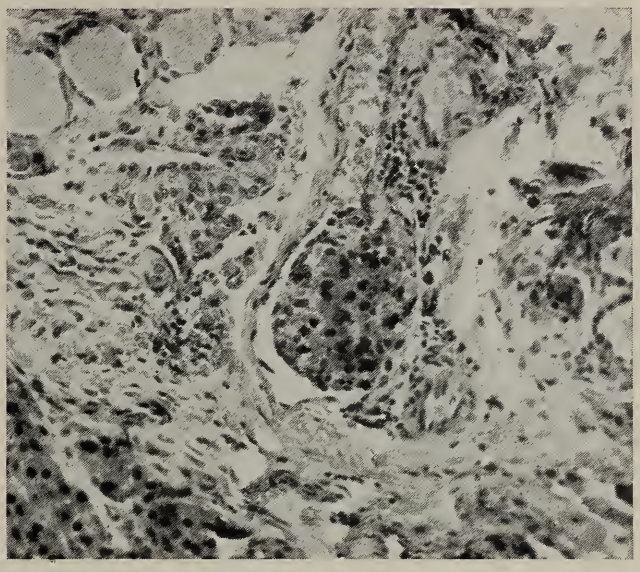


Figure 3.—Magnified 160 times.

SUMMARY

Extirpation of two parathyroid tumors was followed by temporary disappearance of hypercalcemia and bone lesions. Extracts of the tumors produced hypercalcemia in animals. The tissue findings are discussed, particularly in regard to possible malignancy of the adenomas.

Note: The author is indebted to the patient's physicians, Dr. P. A. Taylor and Dr. A. R. Kilgore, for permission to present the pathologic features of this case.

* * *

Addendum: The above paper is reproduced as presented before the pathology section of the California Medical Association under the title "Hyperparathyroidism, Report of a Case Presenting Two Parathyroid Adenomas, Possibly Malignant." Subsequently it was learned that later in May, 1947, operation at the Mayo Clinic revealed local recurrence of tumor and metastases to right lower deep jugular lymph nodes. In both locations the tumor was identical in microscopic appearance to that found at the original operation. The blood calcium level was 17 mg. per cent just before the second operation, then fell to normal postoperatively. The case is still under investigation.

6066 Thornhill Drive, Oakland.

Discussion by E. M. Hall, M.D.

I concur in the diagnosis of "malignant adenoma of the parathyroid" as presented by Dr. Dorgeloh. Well-substantiated malignancies of the parathyroid glands are rare, but this invades the thyroid gland and at least one of the blood vessels, thus setting the stage for metastasis.

A similar tumor was reported by Hall and Chaffin in 1934. A 46-year-old white male had a mass the size of his fist removed from the left side of his neck in March, 1931. The mass was of liver-like consistency except for one part that was cystic. The diagnosis made by another pathologist was "adenoma of the parathyroid and cyst adenoma of the

thyroid gland." The blood calcium was 9.9 mg. per cent and no changes were demonstrated in the bones by x-ray examination. The patient returned to the hospital in November, 1932, with several small recurrent nodules in or near the operative scar. They ranged from 1 to 1.5 cm. in diameter, some of them definitely invading muscle. Microscopic examination revealed not only invasion of skeletal muscle but also a mass of tumor cells within a small blood vessel in the fibrous capsule. Blood calcium and phosphorus determinations were within normal limits. The bones appeared normal in the roentgenogram. The patient was able to return to work and remained well until late in December, 1936. Weakness, night sweats and loss of weight disturbed him during the early weeks of 1937. He developed fever and pain in the chest, and pneumonia was diagnosed. The fever and pain lasted for some three months. By September, when the patient entered the Los Angeles County General Hospital, he had lost 50 pounds in weight. Roentgen examination showed the right lung field almost completely filled with a hazy homogenous density.

The patient died in September, 1938. At autopsy massive tumor metastases were shown to have replaced most of the right lung, and a 3 cm. nodule was present in the lymph nodes at the hilum. Microscopic examination revealed a picture very similar to the tumor seen previously. Here, then, is an instance in which neoplasm similar in cell pattern and in invasive properties to the one reported by Dr. Dorgeloh, finally produced metastases to the lung with fatal outcome. It was four years from the time of the second operation to the onset of symptoms.

It is interesting that bony changes including cystic areas and benign giant cell tumors were present in Dr. Dorgeloh's patient. Of the 20 parathyroid malignancies reported to 1940 only about one in four revealed bone destruction and high serum calcium levels. In a recent report by Alexander, Broders, et al (1944) 12 out of 13 adenomas of the parathyroids reported were considered Grade I adenocarcinomas. It is evident that a less rigid standard is used in classifying this group since malignancy was judged on a basis of cellular anaplasia while no invasion of surrounding tissues or blood vessels was present except in one case.

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Severe Stomatitis Due to Erythema Multiforme — Its Differentiation from Human Foot and Mouth Disease

Saul S. Robinson, M.D., and
Samuel Tasker, M.D., *Los Angeles*

BECAUSE of its varied and protean clinical manifestations, erythema multiforme is of general medical interest. The disease was first recognized in 1817 by Bateman and Bulkley, in 1846, reported the first American cases as "Herpes Iris." Hebra,[3] in 1866, fully described the morphologic features of the eruption under the term "erythema exsudativum multiforme." Hebra was among the first investigators to recognize erythema multiforme to be of internal or systemic origin and not local in causation. Quinquaud ranks priority in describing the mouth lesions in vesiculobullous erythema multiforme. The implication of the viscera in the etiology of erythema multiforme was stressed at the beginning of this century by Osler,[8] who called the internal features of the disease to the attention of the medical world.

Erythema multiforme (Hebra) is essentially cutaneous in location and oral mucosal involvement is present in about 25 per cent of the cases. Rarely, the mucosae of the eyes, nose, esophagus, labia minora, preputium, glans penis, urethra, vaginal tract, cervix and anus are involved.

The association in erythema multiforme, however, of severe vesiculobullous oral mucosal lesions with a paucity of cutaneous lesions has produced confusing and bizarre clinical pictures. In some instances, severe mucous membrane involvement has occurred with entire absence of a skin eruption.[1] Some investigators have described these unusual mucous membrane manifestations of erythema multiforme as new diseases. Thus Rendu, in 1916, termed a severe bullous stomatitis associated with similar lesions on the conjunctival, anal, and penile mucous membranes and a cutaneous vesicular eruption, "Ectodermose Erosive Pluriorificielle." Baader, in 1925, named severe erythema multiforme of the oral cavity associated with cutaneous lesions, "Dermatostomatitis." Stevens and Johnson,[10] in 1922, reported erythema multiforme with predominant involvement of the oral and conjunctival mucous membranes as "a new eruptive fever associated with stomatitis and ophthalmia." This syndrome has also been referred to in the medical literature as "Stevens-Johnson disease." In the erythema multiforme group may also belong the "triple syndrome complex" of Behcet consisting of ulcerations of the oral and genital mucous membranes associated with retinitis and iridocyclitis.

When erythema multiforme is associated with stomatitis, fever, malaise and vesicular lesions on the hands and feet, a clinical picture is produced that resembles foot and mouth disease in man. If this clinical picture occurs in a resident of a dairying or livestock-raising area such as California, where foot and mouth disease epidemics in animals occurred in 1914, 1924, and 1929,[7] it can easily lead to an unwarranted diagnosis of the human form of foot and mouth disease when the clinical diagnosis is unsupported by confirmatory laboratory tests. This close clinical resemblance between erythema multiforme and the human form of foot and mouth disease has been stressed by Klauder[4] and Lever. Internists, pediatricians, ophthalmologists, and dermatologists may especially be called in consultation in cases of erythema multiforme, the choice of consultant depending on the location of the mucous membranes attacked and the constitutional or systemic manifestations predominant. It is the purpose of this article to report a case of severe stomatitis due to erythema multiforme resembling the human form of foot and mouth disease and to differentiate this type of stomatitis from important simulating mouth eruptions.

From the Department of Dermatology of the University of Southern California School of Medicine.

REPORT OF A CASE

The patient, a school girl, aged 15, presented a sore, swollen mouth, malaise, prostration, and fever of 11 days' duration. The mouth eruption began with a painful red spot on the right inner cheek. Blisters and redness soon appeared and spread to involve the tongue, cheeks, throat, and lips. The mouth and throat became so painful and swollen that the patient had difficulty in eating, swallowing, and speaking. Salivation was profuse. The daily temperature had ranged from 99.5° F. to 102° F. since the onset of the illness. About one week after the onset of the stomatitis, red spots and small blisters appeared on the palms, backs of the hands, and the plantar surfaces of the feet. No subjective symptoms were associated with the skin lesions. There was no history of mouth eruption, drug ingestion, or the use of mouthwashes or new dentifrices preceding the onset of the present illness. No other members of the family had suffered from a similar disorder.

Examination. The girl appeared acutely ill and had difficulty in opening her mouth, swallowing, and talking. The breath was fetid. The temperature was 101° F. and the pulse rate 82. Heart, lungs, and abdomen were normal to physical examination. Examination of the mouth and throat showed the mucosae of the lips, cheeks, tongue, hard and soft palate, gums, and throat to be intensely red, swollen and eroded. White denuded hemorrhagic shreds of mucosae were scattered throughout the oral and pharyngeal cavities. A few small vesicles were seen on the hard and soft palates, buccal mucosae, and ventral surface of the tongue. Lymphadenopathy was present in the cervical and sublingual regions. Small macules and vesicles were scattered over the face, palms, dorsa of the hands, fingertips, and plantar surfaces of the feet. Because of previous animal foot and mouth disease epidemics in California, the human form of foot and mouth disease was considered in diagnosis. There was no history of exposure to this infection. Veterinarians informed us that there were no recent reports of the disease in animals in California or nearby areas. Laboratory tests for this disease were nevertheless included in our examination to definitely rule out the possibility of human foot and mouth disease because of the confusing clinical picture.

Laboratory Examinations. Smears from the oral cavity lesions were negative for the presence of Vincent's organisms. Cultures from the mouth and throat grew staphylococcus aureus and streptococcus viridans. Inoculation of a guinea pig's scarified pads with contents of vesicles (Waldmann and Pape's method) was reported negative for the virus of foot and mouth disease by state and federal veterinarians. Blood cultures were negative and the results of the blood count and urine examination were normal. Inoculation of oropharyngeal swabbings and serum from mouth vesicles onto the scarified cornea of a rabbit was negative for the presence of the virus of herpes simplex. The diagnosis was severe stomatitis due to erythema multiforme (Hebra).

Treatment was symptomatic. Soothing alkaline mouthwashes and nicotinic acid (150 mg. daily) were prescribed. Calcium gluconate, 1.0 gr. (15½ grains), was administered intravenously daily. The cutaneous eruption was treated with a soothing calamine shake-lotion.

Course. Twenty-four hours following initiation of treatment the mouth eruption was much improved. The oral swelling and pain had subsided and she was able to open her mouth, chew food, and swallow with less difficulty. The cutaneous eruption, however, had increased in intensity and spread to involve the extensors of the forearms. The patient complained of tenderness of the fingertips, where there were vesicular lesions. During the following ten days the stomatitis and cutaneous eruption gradually subsided and disappeared without leaving residual secondary lesions. The temperature slowly became normal in one week. No recurrence of the stomatitis or cutaneous eruption appeared during the ensuing year while the patient was under observation.



Figure 1.—Severe stomatitis due to erythema multiforme resembling the human form of foot and mouth disease showing swollen lips with erosions.

COMMENT

The diagnosis of typical erythema multiforme (Hebra) is not difficult. There is usually a history of seasonal occurence (spring and fall), provocation of the dermatosis by sunlight, and a tendency of the disease to relapse and recur. The lesions are essentially cutaneous, bilateral, bluish-red, and have a predilection for the face, lateral aspects of the neck, extensor surface of the forearms, and dorsa of the hands and feet. The eruption is commonly erythematopapular or vesiculobullous, and oral lesions, when present, are usually of mild or moderate intensity. Due to the loose structure of the oral mucous membranes and lack of epidermal cohesion, vesicles or bullae in the mouth are rarely found intact, as they break down into superficial erosions. The clinical course of erythema multiforme (Hebra) is usually mild and the patient may suffer from slight malaise, fever, and rheumatoid articular pains. The duration of the disease averages two to six weeks and lesions disappear without sequelae.

Because of simulation of a host of other affections, atypical erythema multiforme primarily attacking the oral mucosae, as in the reported case, may present the greatest difficulties in diagnosis. An aid to the recognition of this type of severe stomatitis may be had by differentiating two important factors that can produce severe erythema multiforme-like simulating manifestations in the mouth and skin—drugs and infection. The ingestion of such drugs as phenolphthalein, antipyrine, barbiturates, and sulfonamides, by susceptible individuals can produce vesiculobullous erythema multiforme-like manifestations of the oral cavity and integument. Rarely, drugs may attack the mouth mucosae without signs of skin involvement and produce a severe stomatitis that may be very difficult to diagnose. Stomatitis due to drugs may also be confusing because of associated fever and



Figure 2.—Severe stomatitis due to erythema multiforme resembling the human form of foot and mouth disease showing involvement of the oral cavity and lips.

constitutional symptoms. In drug stomatitis, however, there is often a history of drug ingestion or sensitivity and an exanthem may show morphologic characteristics of the causative drug. If, however, the drug exanthem is erythema multiforme-like in location and appearance, clinical differentiation between drug sensitivity and erythema multiforme (Hebra) may be impossible and the diagnosis must be deferred until more revealing signs appear.

Among infectious diseases reported to produce the erythema multiforme-like symptom-complex are typhoid fever, streptococcic septicemia, and typhus. Severe stomatitis, however, is rarely associated with these infections and specific diagnostic laboratory examinations (Widal test, blood cultures, Weil-Felix reaction) are of aid in differentiation.

Erythema multiforme of the Hebra type, as illustrated by the reported case, is of unknown origin and is classified as "idiopathic." Some "idiopathic" examples of the disease, however, have been reported to be associated with foci of infection, such as abscessed teeth, or the herpes simplex virus. Keil has summed up the present state of our knowledge of the origin of erythema multiforme (Hebra) by stating that "the etiologic factor or factors in erythema multiforme exsudativum remain to be discovered."

The transmission of the virus of foot and mouth disease to man is rare. Tautwein, in 1932, listed only three cases of human foot and mouth disease in humans that were proven by transfer of the bleb content to susceptible animals. Meyer[6] has pointed out that invariably, during an epidemic of foot and mouth disease in animals, physicians report that they have seen the same infection in man. When careful inquiries are made, however, no conclusive proof is obtainable that the virus of foot and mouth disease was responsible for these reported cases. Meyer states that since a differential diagnosis cannot be made on clinical grounds, the reports of many exanthemata diagnosed as foot and mouth disease without an infection or cross-immunity test are of little value. It is our belief that acute febrile vesiculobullous stomatitis associated with vesicular lesions on the hands and feet, which is confused with human foot and mouth disease, is usually due to erythema multiforme or aphthous stomatitis (herpetic fever).

Ultimate differentiation between severe stomatitis due to erythema multiforme and stomatitis due to the human form of foot and mouth disease is accomplished by means of laboratory procedure. Clinically, the two diseases may be indistinguishable one from the other, inasmuch as the erythema multiforme-like picture may be produced by the filtrable virus of foot and mouth disease. Even tenderness of the finger tips, with vesicular lesions, and limitation of the eruption to mucocutaneous junctions and fingers and toes, as stressed by Sutton, may be present in erythema multiforme and lead to confusion. The virus of foot and mouth disease is found in the vesicle fluid of the lesions and the diagnostic standard laboratory test consists of inoculation of the vesicle fluid in the scarified pads or volar skin of a guinea pig. Positive reaction to the inoculation is appearance of suppurative blebs on the pads in 24 to 48 hours, with eventual extension of the disease to the guinea pig's tongue, lips and palate. Sutton has pointed out that this laboratory test may be performed only by state or federal veterinarians by special permission of the United States Bureau of Animal Husbandry. The nature of the virus also may be demonstrated by cross-immunity tests. Fessler[2] and Richter[9] have outlined the methods which must be chosen to prove the existence of foot and mouth disease virus in the lesions in humans. The importance of the final laboratory infection test was illustrated in the case of our patient, in whom, clinically, the stomatitis and cutaneous eruption due to erythema multiforme was indistinguishable from the human form of foot and mouth disease.

Other types of stomatitis that must be differentiated from stomatitis due to erythema multiforme are stomatitis due to Vincent's infection, aphthous infection, dystrophic epidermolysis bullosa, contact irritants (stomatitis venenata), and pemphigus. Erosive painful stomatitis due to infection by Vincent's fusospirochetal organisms can usually be diagnosed by typical localization of the lesions in the mouth (tonsils and gingivae) and smear examinations. Keil, however, has pointed out that stomatitis due to erythema multiforme as well as other oral diseases may give a positive smear for Vincent's disease. Fusospirochetosis is rarely accompanied by an exanthem and the presence of skin lesions associated with a vesiculobullous erosive stomatitis would tend to exclude the diagnosis of fusospirochetal disease. Therapeutic tests may also aid in the diagnosis of Vincent's infection by the known response of fusospirochetal organisms to oxidizing agents, arsphenamines, and penicillin and the failure of erythema multiforme stomatitis to respond to any specific medication.

The differentiation of aphthous stomatitis due to the herpes simplex virus usually offers little difficulty. Aphthous or herpetic stomatitis is characterized by frequent occurrence in children, discrete papulovesicles that breakdown into painful ulcerations surrounded by an inflammatory halo and a predilection of the lesions for the buccal mucosa, lips, and edges of the tongue. A vesicular generalized exanthem with lesions on the fingers and toes associated with aphthous stomatitis has been reported by Mayer. Inoculation of vesicle fluid or swabbings from the mouth lesions in aphthous stomatitis onto the scarified cornea of a rabbit will prove the presence of the virus of herpes simplex. Typical herpetic vesicles develop within 24 to 48 hours, and this is followed by a purulent keratoconjunctivitis.

Ten cases of aphthous stomatitis simulating human foot and mouth disease were reported by Lebailly in 1921. The differential diagnosis in Lebailly's cases was established by

negative reaction in an attempt to inoculate cattle with vesicle fluid of the mouth lesions. Dystrophic epidermolysis bullosa may cause erosive oral cavity lesions simulating stomatitis due to erythema multiforme. The differential diagnosis, however, is not difficult, as dystrophic epidermolysis bullosa occurs in early childhood, is familial in occurrence, and is associated with cutaneous lesions due to mechanical trauma at sites of pressure. Characteristic atrophy and scarring occur at the site of healed lesions in the oral cavity and skin in this disease and are absent in erythema multiforme.

Chemical irritants may produce vesiculobullous and erosive stomatitis venenata. These irritants can be found in dentifrices, dentures, and mouthwashes. The history of use of mouth irritants, performance of patch tests with offending substances, lack of constitutional symptoms, and the absence of an erythema multiforme exanthem will aid in the differentiation.

In the early stages of an erosive bullous stomatitis, before the appearance of an exanthem, pemphigus and erythema multiforme may be impossible to differentiate clinically. The course of the disease, the appearance of typical erythema multiforme skin lesions with absence of "Nikolski's sign" in the skin, and a negative phytotoxic test (Pels-Macht) would aid in excluding pemphigus in the differential diagnosis. At times, however, the differentiation of stomatitis caused by these two diseases is very difficult, if not impossible, and can only be made after prolonged observation of a particular case.

The treatment of stomatitis due to erythema multiforme is symptomatic. Inasmuch as the cause of the disease is unknown, medicaments recommended in its treatment are employed empirically. The value of epinephrine, salicylates, alkalinization, calcium, sulfanilamide and local topical applications[5] in erythema multiforme is disputable. The favorable reports found in the medical literature of response of the disease after the use of these agents cannot be evaluated without controls, as erythema multiforme is a self-limited eruption.

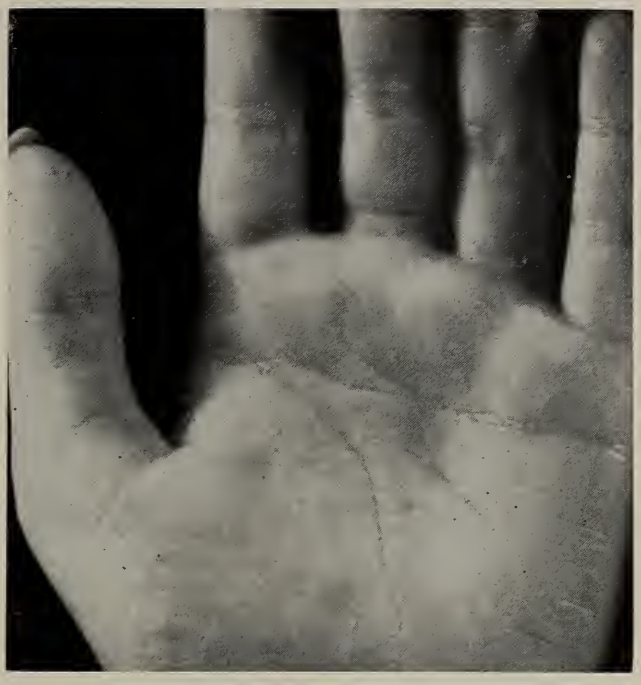
The prognosis of severe stomatitis due to erythema multiforme varies according to the complications that may appear due to spread of the disease from the oral cavity into the larynx, tracheobronchial tract, lungs, and esophagus. Fatalities have been reported in severe cases due to bronchopneumonia secondary to tracheobronchial tract involvement. Uncomplicated erythema multiforme stomatitis is a self-limited disease that usually clear in two to four weeks without sequelae. Recurrence of seasonal type and relapse, however, is a frequent and characteristic finding in erythema multiforme and prognosis as to absolute cure in any particular attack of the disease involving the oral cavity or skin must be guarded.

SUMMARY AND CONCLUSIONS

A case of severe stomatitis due to erythema multiforme resembling the human form of foot and mouth disease is reported.

Severe stomatitis due to erythema multiforme produces a clinical picture that may lead to confusing it with the human form of foot and mouth disease unless standard diagnostic laboratory procedures of infection and cross-immunity tests are performed. Proven cases of the human form of foot and mouth disease are rare and physicians should be cautious in making this diagnosis without laboratory proof in a patient suffering from severe febrile vesiculobullous stomatitis associated with vesicular lesions on the hands and feet.

Other forms of stomatitis differentiated from stomatitis due to erythema multiforme are those due to drugs, Vincent's disease, aphthae, dystrophic epidermolysis bullosa, contact irritants (stomatitis venenata), and pemphigus.



Vesicular lesions of erythema multiforme on the hand resembling the human form of foot and mouth disease.

The varied mucosal and constitutional manifestations of erythema multiforme have produced unusual clinical pictures that have been described as "new diseases" in the medical literature. To avoid confusion, these so-called new diseases should be recognized and properly classified as atypical erythema multiforme.

1930 Wilshire Boulevard.

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CLINICAL SYMPOSIUM

Prepared under the direction of Edgar Wayburn, M.D., *San Francisco,* and Clarence J. Berne, M.D., *Los Angeles*

Palliative Management of Mammary Carcinoma

Ian Macdonald, M.D.
Associate Clinical Professor in Surgery

Lewis W. Guiss, M.D.
Instructor in Surgery

Dr. Macdonald:

SURGICAL literature on mammary carcinoma is so largely concerned with the radical, curative approach to the disease that one is apt to forget that half or more of all women with this neoplasm are incurable when first examined. Further, there are certain forms of breast cancer which are technically operable but biologically incurable, and in which radical mastectomy may be harmful. The palliative management of this neoplasm is, therefore, as important statistically as the surgeon's attack on the potentially curable lesions.

The palliative results achievable in cancer of the breast are frequently impressive, for women can live with the disease effectively controlled for five to ten years or longer and continue to be socially and economically useful members of society. Not infrequently such prolongation of life is of immense importance to the family unit with young children. With an estimated 70,000 current cases of breast cancer in the United States, the clinical management of these patients is a recurring problem in general practice. The cooperation of physician, radiation therapist and, less often, the surgeon constitutes the desirable liaison in this problem.

CRITERIA OF INCURABILITY

Of first importance in establishing indications for palliative management are the criteria which determine incurability. Essentially, these criteria are those which make the patient ineligible for radical mastectomy, and are based either on the stage of the disease or its pattern of growth, as follows:

(A) A far advanced primary lesion in the breast.
(B) Extensive regional metastases.
(C) Distant metastases.
(D) Evidence of a highly malignant, rapidly growing, biologically incurable lesion.

Reducing these basic factors to specific situations, an arbitrary outline by which one may determine incurability can be offered.

DETERMINING FACTORS

(A) Extent of Primary Lesion

1. *Extensive skin involvement.* Minimum skin attachment or retraction may be due to a scirrhus, superficially located tumor with dermal or subdermal sclerosis. Actual skin involvement means extensive permeation of local lymphatics and is as grave an omen as supraclavicular nodal metastases. "Peau d'orange" is a sign of late cancer. Satellite nodules in adjacent skin are a particularly bad sign.

2. *Fixation to pectoral fascia or chest wall.* Also a sign of late cancer, for if the disease has reached the pectoral fascia it is also in the subpectoral lymphatics and thus beyond the deepest plane of chest wall dissection in radical mastectomy.

3. *Ulceration of skin.* Full thickness ulceration of any extent is usually a sign of inoperability, except in some slowly growing lesions without evidence of regional nodal metastases. In elderly women even with extensive ulceration the breast may be fully mobile and the regional nodes clear.

4. *Extension beyond the midline.* Occasional inner quadrant lesions near the medial periphery of the breast will have infiltrated across the midline, thus gaining access to the lymphatic system of the contralateral breast and axilla. This is an added hazard with inner quadrant lesions which frequently metastasize in the region of the internal mammary circulation.

(B) Extensive Regional Metastases

"Regional" lymph nodes include axillary and infra-clavicular groups. Supraclavicular nodes are distant, not regional.

1. *Bulky, fused axillary nodes.* Not an absolute contraindication to radical surgical treatment, especially if low in axilla or retropectoral. Fused nodes mean metastases no longer contained within intact lymph nodes, are practically synonymous with distant metastases and should have at least a trial with x-radiation.

2. *Extensive apical axillary nodal enlargement.* Sizable nodes at axillary apex are nearly certain indications of more distant spread.

(C) Distant Metastases

1. *Supraclavicular lymphadenopathy.* Metastases to nodes above the clavicle are as certain a sign of incurability as is mediastinal node involvement. Enlarged supraclavicular nodes which are suspect, in otherwise operable cases, should be excised for histologic verification before radical operation on the breast.

2. *Pulmonary and Mediastinal.* Routine preoperative chest films should be obtained in all cases in which breast tumors which may be malignant are present.

3. *Skeletal. Order of Frequency:* (1) Ribs; (2) Spine (a) Lumbar, (b) Dorsal, (c) Cervical; (3) Pelvis; (4) Upper Femora; (5) Skull; (6) Humeri. Early metastases to bone are frequently not radiographically apparent. Preoperative skeletal surveys by x-ray are not mandatory except in the presence of persistent pain in possible metastatic sites.

4. *Hepatic.* May be apparent by examination. More frequent in inner quadrant lesions.

5. *Cerebral.* Headache or visual disturbance of progressive sort are usually present.

6. *Other sites.* Uncommon, usually not demonstrable.

(D) Biologic Incurability

Certain forms of mammary carcinoma, approximately 8 to 10 per cent of all cases, are from the beginning rapidly growing and metastasizing and almost invariably lethal in two years or less. Two such lesions distinguished by certain clinical features, and which usually are not benefited by radical operation, may be recognized.

1. *Lesions developing during pregnancy or lactation.* The majority of these neoplasms are rapidly growing, with early regional and frequently distant metastases. Should be treated primarily by x-radiation.

From the University of Southern California General Tumor Surgical Service, Los Angeles County Hospital.

2. *"Inflammatory" carcinoma.* So-called because of resemblance to acute inflammation of breast, with erythema of overlying skin. Such lesions may involve most of the breast in a few weeks. Primary lesion and local metastases are well controlled by x-radiation. Most of such patients die from distant metastases. Radical mastectomy seems to disseminate the disease more rapidly in some instances.

3. *Other anaplastic lesions.* Rapid growth of the primary lesion, or large axillary metastases even with a small breast lesion, may indicate a highly malignant, incurable neoplasm.

Other considerations related to the patient as a biologic unit may constitute inoperability. Severe cardiovascular disease is probably the most common. As in other concurrent disease, the risk must be measured in terms of expected longevity in relation to the anticipated progress of the breast cancer. Age in itself is not a contraindication to radical mastectomy, for many women in their eighth decade developing cancer of the breast have survived that long by reason of a constitutional integrity that enables them to withstand the operation.

ADAPTATION OF PALLIATIVE TREATMENT IN TERMS OF GROWTH PATTERN

From the foregoing outline it is apparent that mammary carcinoma is so variegated in its pattern of local growth and metastases that the palliative program must vary to a similar degree. In one patient the problem may be the reduction of growth of the tumor or the healing of ulceration in the breast, so that the impending terminal phase of the disease from distant metastases may be made less distressing. In another the problem may be that of an advanced local lesion of long duration, dilatory growth characteristics and without evidence of distant metastases, in which eradication or control of the local lesion may prolong life by years rather than months. In still others, the problem is that of palliative treatment of metastatic lesions, particularly in bone where adequate control of the disease may result in several more years of useful activity.

The measures available for the effective palliative treatment of breast cancer are still headed by x-radiation, both for the primary and secondary sites. Interstitial radium may be of value in occasional cases. Local surgical measures are of great value in selected patients, and combination of them with irradiation is often indicated. The use of sex hormones is still in an investigative phase, but present knowledge suggests that their status will be as complementary agents to irradiation. There are some distinct hazards in the large doses of androgenic and estrogenic hormone required for effective treatment, but the value of these agents in carefully selected patients, at certain age periods, seems amply demonstrated. The effectiveness of hormonal treatment is, however, highly variable, and the considerable number of therapeutic failures encountered should do much to discourage the premature popularity these agents now enjoy. Otherwise, palliative management requires in the later stages of the disease specific measures for a variety of complications, and an intelligent use of analgesic drugs on a progressive scale of effectiveness and dosage.

As encountered by the clinician, patients for palliative management may be bracketed as follows:

1. *Primary Cases*
 See groups A, B, C, D above
2. *Secondary (Post-Operative) Cases*
 Local Recurrence
 A. Chest Wall—10-25 per cent of post-operative cases
 B. Axillary—5-8 per cent of post-operative cases
 C. Distant Metastases—See Group C above

CLINICAL MANAGEMENT

Dr. Guiss:

1. *A, B, D. Primary Local and Regional Disease*

The control of inoperable primary carcinoma of the breast with or without axillary metastases is basically a problem of management with x-ray therapy. X-ray ports are outlined over the primary lesion in such a way that the tumor can be crossfired through at least two ports, care being taken to irradiate as little lung tissue as possible. The axillary and supraclavicular metastases can also be crossfired in a similar way. It is often possible to bring the local and regional disease under clinical control for long periods of time. Five-year survivals without apparent disease have occasionally been obtained in this group of cases but are, of course, unusual. If the patient is young, as she often is, particularly in the biologically incurable group, x-ray castration should be part of the course of x-ray therapy. When there is extensive skin ulceration with associated infection and risk of hemorrhage, the patient not only presents a serious nursing problem but also technical difficulties in irradiation. Frequently it is preferable to do a simple mastectomy, thereby removing the foul, ulcerating mass before x-ray treatment is begun. It is usually possible to close the skin flaps but if necessary a split thickness graft may be utilized to close the defect. The care of the patient is thus much simplified and the palliative end result will be improved.

2. A. *Post-operative Skin and Chest Wall Recurrence*

It is generally agreed that if extensive post-operative skin or chest wall recurrence develops after a properly performed operation, the disease was not primarily operable, for of course it is not always possible to tell from a clinical standpoint whether a lesion is actually operable or not. If there are but one or two skin metastases, local excision of these lesions with a reasonable margin of normal tissue is probably justified. The treatment of choice, however, is x-radiation. One or two individual metastases in the skin can be treated by small ports using low voltage x-ray. However, since metastases are usually multiple, as a rule it is preferable to treat the entire operative area in which further skin nodules might be expected to develop. Radium needles can be inserted into areas in which there is recurrence in the skin, but there is always the danger of permanent injury to underlying bone and cartilage which sometimes

gives the patient more difficulty than the skin lesions themselves. Recently, some patients with recurrences in skin and soft tissue have been treated with high doses of estrogenic materials, and in some instances this has been followed by complete regression of the clinically apparent disease. Estrogenic therapy probably should be reserved for skin or soft tissue recurrence in elderly women many years post-menopausal who have already received x-radiation and whose skin cannot tolerate further therapy.

C. 3. *Skeletal Metastases*

The pain incident to skeletal metastases from breast carcinoma is somewhat variable, depending upon the extent and location of the lesions. There may be very extensive bone destruction without any symptoms at all. Occasionally, the first suggestion of bone metastases is a pathological fracture. More often the patient will complain of a dull ache of variable intensity, often worse at night and usually responding at first to mild analgesics. The symptoms of metastases to the spine are often mistaken for those of arthritis until x-ray films show the true nature of the process. Progressive collapse of the vertebral bodies causes pressure on the adjacent nerves, and symptoms of radiculitis then are added to the duller pain of the local disease. At times the patient may complain of severe pain in one of the bones and there may be nothing evident on radiographic examination. It is usually safe to assume in such cases that there is a metastasis present even in the absence of x-ray findings. Early bone metastases are not detectable by x-ray examination. By the time metastatic areas in the bone are discernible by x-ray examination, advanced destruction is present.

Despite the recent wave of enthusiasm for treatment of bone metastases by androgenic therapy, x-radiation still remains the treatment of choice for such lesions. Not only is the relief from pain prompt and lasting but also it is usually possible to arrest the progress of the metastatic lesion, often with complete recalcification. If the patients are pre-menopausal castration is usually indicated. Since x-ray castration seems to be as effective as surgical castration and is far more simply accomplished, it has largely replaced the surgical procedure. Androgenic therapy for skeletal metastases is currently popular. It may be used in any case regardless of the age of the patient. Dramatic response, often apparent within two or three weeks, is usually characterized by relief of pain, increased appetite, gain in weight and a sense of well-being. Unfortunately, the clinical progress of the patient may not parallel the symptomatic improvement and sometimes the metastatic lesions progress rapidly despite the symptomatic palliation. Calcium and Vitamin D have been administered in large quantities in an effort to facilitate the calcification of bony metastases but the end result of this additional therapy has not been convincing and the administration of these agents probably is not justified. In those cases in which there are metastases in the vertebral bodies, a properly fitted back brace will not only give the patient a great deal of relief from pain but will also protect the injured vertebral bodies from further strain thereby retarding progressive collapse of the bodies and permitting recalcification to take place following x-ray therapy or x-ray and androgenic therapy.

C. 2. *Pulmonary, Mediastinal and Pleural Metastases*

Occasionally, solitary and well localized metastatic deposits in the lungs may be treated by deep x-ray therapy. The results are unpredictable but at times the metastatic lesion may shrink to a fraction of its former size or entirely disappear. As a rule, pulmonary metastases are multiple and when the pleura becomes involved there is usually associated pleural effusion. If the amount of fluid is small, drainage is not necessary but if the vital capacity of the patient is interfered with by the volume of effusion, thoracentesis will afford a great deal of comfort. This procedure can be done either in the home or the office without the use of expensive or complicated apparatus.

There are isolated reports of regression of pulmonary metastases following both androgen and estrogen therapy, but use of these agents for the control of pulmonary metastases alone does not seem justified.

C. 4. *Liver and Other Abdominal Metastases*

The treatment of metastatic abdominal deposits from breast carcinoma is discouraging. When ascites develops the patient is not only subjected to abdominal discomfort but there is also elevation of the diaphragm with consequent impairment of vital capacity which may have been diminished already by pulmonary disease. Removal of the ascitic fluid as it collects will not only prevent abdominal discomfort but will relieve dyspnea in a patient with an already diminished vital capacity. Hormone therapy has not been used for the treatment of ascites. Recently we have seen a patient with extensive soft tissue recurrence associated with ascites. She was given high doses of estrogenic substance in the hope that this would control the skin recurrence. There was prompt regression of the skin metastases, and concommitantly the ascites was apparently competely absorbed, suggesting that there was regression of the intra-abdominal metastases also.

C. 5. *Cerebral Metastases*

Symptoms and signs incident to cerebral metastases depend entirely upon the location of the metastatic lesion. Careful neurologic examination may localize the metastatic deposit quite accurately. In cases where the progress of the disease appears slow and it is possible accurately to determine the site of the metastatic process, it is sometimes feasible to give deep x-ray therapy through small ports to the involved area. Results are extremely variable, but sometimes worthwhile palliation may be obtained.

SPECIAL CONSIDERATION OF MANAGEMENT

Hormone Therapy

The exact role of hormone therapy in the palliative treatment of mammary carcinoma is as yet unknown. It is at present on an experimental basis and care should be taken to be sure that the patient is benefited

rather than injured by such treatment. In light of the facts now known, it appears that patients with metastatic lesions in bone, without regard to age, are entitled to a trial of androgenic therapy. (Such treatment, however, has not replaced the known beneficial results that can be obtained by X-ray therapy to such lesions.) The dosage is usually 100 mg. of testosterone propionate given three times a week until a total of 3600 mg. has been administered, after which the patient is placed on a so called maintenance dose of 100 mg. weekly for an indefinite period. Symptomatic relief, usually apparent within two or three weeks, is characterized by relief of pain, gain in weight, increased appetite, diminished requirement for narcotics and a general sense of well-being. Objective signs of improvement do not necessarily parallel the relief of pain. Androgenic therapy must be controlled by roentgenographic and blood chemistry studies. In favorable cases there may be X-ray evidence of remineralization of the bone, but sometimes this does not occur even though there are subjective signs of benefit. Occasionally, the administration of high doses of androgen will increase the rate of bone destruction, and of course the medication should be stopped promptly in these cases. In the presence of a high value for serum calcium, treatment should be given cautiously. If the serum calcium drops to normal levels a good result can be expected; however, if it remains at a high level or a previously low serum calcium becomes elevated, androgenic therapy should be terminated at once.

Certain masculinizing effects are usually evident with such high dosage of testosterone. These include hirsutism, coarsening of the skin, voice change and often an increase in libido. These changes are most marked in younger women and may be so undesirable to the patient or to the family that continuance of testosterone therapy is not permitted. Occasionally, a patient, especially with high value for blood calcium, becomes intolerant to the drug, developing severe nausea, vomiting and other signs of intolerance, and of course androgenic therapy is not suitable for such patient.

Indications for the palliative use of estrogenic therapy are not yet definite. The information at present available suggests that estrogenic therapy should be reserved for patients in the older age group with soft tissue involvement. Beneficial effects have been largely restricted to regression in the size of inoperable primary lesions and in regression of soft tissue metastases. There appears to be also an improvement in the general physical condition of the patient. This favorable response, when it occurs, appears to be temporary and highly unpredictable. The preparation most commonly used is diethylstilbestrol given orally in doses of 15 mg. daily. Many patients do not tolerate the drug well. Estrogenic therapy should never be used for patients below the age of 60; in pre-menopausal women the administration of it may even accelerate the progress of mammary carcinoma. Frequently large doses of estrogens produce uterine bleeding, necessitating a diminution in the amount of the drug used.

Analgesics and Narcotics

Properly administered X-ray therapy is probably the most effective method of pain control in advanced cases of mammary carcinoma. When X-ray therapy is no longer effective and it is necessary to supplement its effects by medication, care should be taken in choosing a suitable drug. Many patients, particularly in the older age group, can be expected to live for months or years, and it is wise to reserve the stronger narcotics until they are absolutely necessary. As a rule, aspirin compounds supplemented with codeine are sufficient. Sometimes even aspirin alone will control the early pain. It is often possible to carry the patient on increasing doses of aspirin compounds with codeine up to the terminal stages of the disease. The large amount of codeine required not only diminishes the appetite but also constipates the patient, making special attention to bowel evacuation necessary. When codeine is no longer effective, a change can be made to either demerol, metapon or dilaudid, the choice depending upon the personal preference of the physician and the individual response of the patient to the drug. Some patients have less intolerance for one of the drugs than for another. Methadon, a new synthetic preparation, in doses varying from 2.5 to 10 mg. has been highly effective in the control of pain in the more advanced cases. The drug is less inclined to cause addiction than some of the others and does not interfere with the appetite, is less constipating and is quite inexpensive. Morphine with its euphoric and hypnotic effects should be reserved for the terminal stages of the disease.

Specific Measures for Pain Control

When there is severe pain originating in areas served by the lumbar and sacral levels of the spinal cord, intrathecal injections of alcohol will often give marked relief over a period of weeks or months. This procedure is of greatest value in cases where the pain is unilateral in distribution, although it may still be utilized when the pain is bilateral. The procedure is quite simple, but not without occasional undesirable sequelae such as disturbances in bladder and anal sphincter control, muscle paralysis and other undesirable complications. Severe localized pain such as that found in association with pathological fractures of the ribs can be effectively controlled by nerve block using one of the synthetic agents dissolved in oil for prolonged relief. Sometimes alcohol injections of individual nerves can be utilized to advantage. Cordotomy, an operative measure in which the spino-thalamic tract is severed, should be reserved for patients whose pain is severe and whose life expectancy exceeds at least six months. The operation, which is technically difficult and carries a certain amount of risk, should be done only on those patients in whom the measure of palliation would justify the procedure. Prefrontal lobotomy is a relatively new operation which has been recommended for intractable pain in certain selected cases. Application of the procedure has been quite limited, and it should be reserved for unusual cases.

MEDICAL PROGRESS:

Isotopes in Clinical and Experimental Medicine

ELLSWORTH C. DOUGHERTY, Ph.D., M.D., and JOHN H. LAWRENCE, M.D., Sc.D., *Berkeley*

This is Part II of an article in two parts. Part I appeared in the July issue of California Medicine, and with it were the list of references for the entire article and the Table 1 referred to in the following text.

IMPORTANT APPLICATIONS OF ISOTOPES IN EXPERIMENTAL MEDICINE

General Considerations:

In experimental medicine much the largest part of the work with isotopes has involved their use as tracers. The volume of work in which isotopes have been applied to studies on the biological effects of radiation has been by comparison rather slight. In this section we are limiting ourselves, except in passing comment, to a brief survey of some of the more important tracer studies.

So far investigations have been carried out with stable or radioactive isotopes of 56 of the 96 known elements. The metabolism of most elements known or thought to be essential to living systems has been investigated in varying degree with one or more isotope. In the case of elements known or thought to be necessary in mammalian nutrition ($_1$H, $_6$C, $_7$N, $_8$O, $_{11}$Na, $_{12}$Mg, $_{15}$P, $_{16}$S, $_{17}$Cl, $_{19}$K, $_{20}$Ca, $_{25}$Mn, $_{26}$Fe, $_{29}$Cu, $_{53}$I, probably $_{27}$Co and $_{30}$Zn, and possibly $_{35}$Br) some tracer studies have been made on mammals with isotopes of all except $_{12}$Mg; in fact, only one biological problem, i.e., photosynthesis in higher plants (Ruben, Frenkel, and Kamen[117]), has so far been attacked using a $_{12}$Mg isotope—the radioactive species, $_{12}Mg^{27}$. Work with the stable isotopes, $_1H^2$ (D), $_6C^{13}$, and $_7N^{15}$ has been very extensive, while but little use has thus far been made of the stable isotopes $_8O^{18}$ and $_{16}S^{34}$. Fairly or very extensive studies have been carried out with the radioactive species $_{11}Na^{24}$, $_{15}P^{32}$, $_{16}S^{35}$, $_{17}Cl^{38}$, $_{19}K^{42}$, $_{20}Ca^{45}$, $_{26}Fe^{55}$, $_{35}Br^{82}$, $_{53}I^{130}$, and $_{53}I^{131}$ among elements known or thought to be essential for mammals and with $_{38}Sr^{89}$, which, though not representing an essential element, so far as known, has been used as a substitute for a $_{20}$Ca isotope by reason of the poor yields and difficulties in the measurement of $_{20}Ca^{45}$. Some tracer work has also been done with such unstable species as $_1H^3$ (T), $_6C^{14}$, $_7N^{13}$, $_{11}Na^{22}$, $_{25}Mn^{52}$, $_{25}Mn^{54}$, $_{25}Mn^{56}$, $_{27}Co^{56}$, $_{27}Co^{58}$, $_{29}Cu^{64}$, $_{30}Zn^{65}$, and $_{53}I^{128}$, among the essential elements. Of these, T and $_6C^{14}$ are unquestionably finding extensive use in current research, not yet published upon. In addition a few tracer studies have been carried out on mammals using radioactive species of a number of other elements (some 33) not known or believed to be essential to man; these are listed in Table 1. Studies have also been carried out with isotopes of the non-essential elements $_3$Li, $_5$B, and $_{80}$Hg; but in the case of the first two these have been non-tracer experiments with stable species ($_3Li^6$ and $_5B^{10}$), and the radioactive isotope $_{80}Hg^{197}$ has so far been applied only to the determination of the amount of Hg vapor contaminating the atmosphere of an industrial establishment where mercury was used (Goodman, Irvine, and Horan[40]). In addition there have been extensive toxicological studies with $_{88}$Ra and $_{92}$U.

From the foregoing paragraph it may be seen that a great deal remains to be done with tracers in essentially preliminary work on mammalian metabolism. Aside from the 45 elements for which such isotopic studies are lacking, a number of essential elements have been little more than touched—$_{25}$Mn, $_{27}$Co, $_{29}$Cu, and $_{30}$Zn. These are "trace elements," and it seems likely that significant advances in our understanding of their metabolic role will come only with development of methods for their study with isotopic tracers. Other elements also deserve intensive investigation; for example, nickel ($_{28}$Ni), a possibly essential nutrilite, has not been studied isotopically at all, although this deficiency is sure to be soon corrected.

In general, radioactive isotopes offer simpler techniques of application to biological problems than do stable isotopes. This is because the Geiger-Müller counter, with which most of the former may be detected quantitatively, is simpler of operation than the mass spectrometer, with which the latter (except for D and $_8O^{18}$) must be measured. Unfortunately, important elements such as $_7$N, $_8$O, and $_{12}$Mg have no unstable isotope of sufficiently long half-life to permit their use in any but very short tracer experiments. However, useful stable species exist for $_7$N and $_8$O at least, and probably the two rarer species of $_{12}$Mg will also prove very valuable.

In the following subsections the more important studies with isotopes are grouped according to broad categories of elements based upon the significance of the latter in metabolism.

Studies on Elements Constituting the Major Organic Metabolites:

Introduction. The elements that constitute the major organic metabolites include principally $_1$H, $_6$C, $_7$N, $_8$O, $_{15}$P, and $_{16}$S. Other elements, of course, play important roles in intermediary (i.e., organic) metabolism, but for the purposes of this discussion we are limiting ourselves to the foregoing six.

The use of isotopes as labels of intermediary metabolism was originated by Schoenheimer over a decade ago. He established clearly an important concept—the dynamic state of organic body constituents; in other words, that carbohydrates, fats, proteins, etc., are undergoing a continuous process of breakdown and resynthesis in the living cell, even seemingly inert substances such as stored body fats (see Schoenheimer[122]).

Carbon. Three isotopes of ${}_6C$ have been used in biological work—${}_6C^{11}$ (20.5 minute half-life), ${}_6C^{13}$ (stable), and ${}_6C^{14}$ (>5,000 year half-life). The first is adaptable only to short-term experiments, whereas the latter two can be used for prolonged studies.

${}_6C^{11}$ has found important application in the study of CO_2 utilization by animals and plants (Buchanan and Hastings[12]; Werkman and Wood[149]; Wood[151]; Ruben and Kamen[119, 120]) and on carbon monoxide metabolism (Tobias *et al.*[141]). The latter authors have shown that $C^{11}O$ is not converted to $C^{11}O_2$ *in vivo* in the human during a period of two hours. An advantage that C^{11} has over C^{14} is the fact that the penetrating annihilation gamma rays of the former permit convenient *in vivo* measurements whereas the weak beta rays of the latter permit *in vitro* counting only, which for reasonable accuracy must have a rigidly controlled geometry.

${}_6C^{13}$ has been used in a rather large series of experiments dealing with the intermediary metabolism of carbohydrates, fats, and, to a lesser degree, amino-acids (Buchanan and Hastings[12]; Vennesland[145]).

${}_6C^{14}$ has only recently become available in appreciable quantities—from the nuclear pile reactor—and has not yet had widespread application insofar as published reports are concerned, although the literature is growing rapidly. It promises to be one of the most important of tracer isotopes in studying intermediary metabolism. As examples of the type of syntheses that will become increasingly common may be mentioned the recent work of Reid[113] in synthesizing labeled tyrosine, of Heidelberger *et al.*[55] in synthesizing labeled dibenzanthracene (an important aromatic carcinogen), and Melville, Rachele, and Keller[97] in synthesizing methionine with C^{14} in the methyl radical. Recently Bloom, Curtis, and McLean[8] have shown that ${}_6C$ administered as carbonate may be laid down at least for several weeks in bone without showing any change in concentration. However, many organic compounds containing labeled ${}_6C$ apparently are metabolized very rapidly and do not remain long in the body.

Hydrogen. The two tracer isotopes of ${}_1H$— deuterium or D (stable) and tritium or T (about 30 year half-life)—have approximately the same role to play in studies on metabolism except that a considerable increase in sensitivity of measurement is possible with compounds labeled with T over that with compounds labeled with D.

D has been used to label a wide variety of organic compounds (Schoenheimer[122]; Kamen[70]). It has also been used by Hevesy and Hofer in the form of "heavy water" in the study of the turnover of body water[61-63] and also in the determination of body water content by the isotope dilution method. These workers found that while a little deuterium appears in the urine within half an hour after ingestion by mouth, the bulk of the water in the body as determined by labeling with heavy water has a half-life of about 9 days, or, otherwise stated, that a given water molecule spends, on the average, about 13 days in the body. Recently Moore[99] with D and Pace *et al.*[107] with T, have also determined total body water in man. In view of the fact that there is no other reliable method for the determination of body water, these isotopes certainly will find wide usefulness in this connection.

T as an organic labeling agent has so far been used only in studies on photosynthesis (Norris, Ruben, and Allen[106]). However, it, as well as D, doubtless has great potentialities in the further unraveling of the vast complexities of intermediary metabolism.

Oxygen. No studies with ${}_8O$ isotopes have as yet been carried out in mammalian physiology. ${}_8O^{18}$ (stable) may be expected to play an important role.

Nitrogen. Of the two isotopes of ${}_7N$ and adaptable to tracer work—${}_7N^{13}$ (10.13 minutes half-life) and N^{15} (stable)—only the latter has had wide application. N^{13} has been used to study respiratory gas exchange by Jones[66]. N^{15} has been widely used in the study of the intermediary metabolism of amino-acids and proteins (Vennesland[145]).

Phosphorus. There are more publications dealing with the one useful tracer species of ${}_{15}P$—${}_{15}P^{32}$ (14.3 day half-life)—than with any other isotope, stable or radioactive. The reason for this lies in the relative ease with which it can be produced (even by bombarding phosphorus with neutrons from a radium-beryllium mixture) its convenient half-life, and the simplicity with which it can be measured (because of its penetrating beta rays).

The major tracer studies with ${}_{15}P^{32}$ intermediary metabolism have been on the formation and fate of two important classes of organic compounds; the phospholipids (Chaikoff and Zilversmit[13]) and the nucleoproteins (Hevesy[59]). The liver has been shown to be the main site of phospholipid production for systemic use, although the kidney and intestinal mucosa synthesize their own phospholipids independently of the liver. Considerable work has been done on the turnover of ribose- and desoxyribosenucleic acid in various tissues. It has been demonstrated that the distribution of labeled phosphate (introduced in the inorganic form) in the nucleic acid moiety of nucleoproteins correlates with the known metabolic activity of the various tissues.

${}_{15}P^{32}$ has also been used in the study of the mineral metabolism of phosphorus (Chievitz and Hevesy[15, 16]; Hevesy, Hahn, and Rebbe[60]). A slow but definite turnover of bone phosphates has been clearly shown. Phosphate excretion is now known to take place through both urine and feces, although less than 10 per cent escapes by the latter route.

Techniques for labeling erythrocytes with ${}_{15}P^{32}$ are known and have been used by Næslund and

Nylin[103] to show that the human placenta in rare cases is permeable to these cells. Labeled cells introduced into the maternal circulation before parturition were later detected in the fetal cord blood. This study may have great significance in relation to the Rh problem.

Sulfur. The two isotopes of $_{16}S$ that have been used in tracer experiments are $_{16}S^{34}$ (stable) and $_{16}S^{35}$ (87.1 day half-life).

Heavy sulfur—$_{16}S^{34}$, the most abundant of the three rarer isotopes of $_{16}S$—has thus far been produced in small amounts only and consequently has had very limited use. Du Vigneaud *et al.*[26] have synthesized labeled methionine using $_{16}S$ slightly enriched with $_{16}S^{34}$, as well as $_{6}C^{13}$ (heavy carbon) in the beta-position; these workers were able to show with this doubly labeled material that the $_{6}C$ chain of methionine is not utilized in the *in vivo* conversion of methionine to cystine.

Radiosulfur—$_{16}S^{35}$, the only unstable species of $_{16}S$ of convenient half-life for biological use—has also had limited application, although somewhat more extensive than $_{16}S^{34}$. Its use has been reviewed by Kamen[70]. A number of studies have been carried out in both plant and animal sulfur metabolism. Particularly important has been the work of Tarver and his associates (Tarver and Reinhardt[134]; Tarver and Schmidt[135-137]; Melchior and Tarver[95, 96]) on the synthesis of $_{16}S$-containing amino acids and the metabolism of these and of elemental sulfur in mammals, including the *in vivo* conversion of methionine to cystine and taurine and the distribution of sulfur fed as methionine in the body protein. Most significant of the results of their work and the work of other biochemists using the sulfur label has been the further verification of the dynamic state of body constituents, for a rapid turnover of protein $_{16}S$ has been demonstrated, even in the fasting animal. Neither elemental $_{16}S$ nor sulfate can be used to form $_{16}S$-containing amino acids. Soluble sulfides are mostly converted to sulfate and thus share the fate of the latter, although a small amount of sulfide may be incorporated into protein as shown by Smythe and Halliday[129] and by Dziewiatkowski[27].

Studies on Elements Constituting the Major Mineral Metabolites:

Introduction. For our purposes here we are considering the following five elements as constituting the major mineral metabolites: $_{11}Na$, $_{12}Mg$, $_{16}Cl$, $_{19}K$, and $_{21}Ca$; of these, $_{12}Mg$ has as yet received no study with tracers in mammalian physiology. $_{1}H$, $_{6}C$, $_{8}O$, and $_{15}P$ are also, of course, of major importance in mineral metabolism, but have already been considered in the preceding subsection.

The study of mineral metabolism with tracers began in 1935 with the work of Chievitz and Hevesy[15] on $_{15}P$ uptake and distribution in the rat. Since that time a considerable literature has grown up, particularly in regard to electrolyte dynamics and bone metabolism.

Electrolytes. Kamen[70] has reviewed the available radioisotopes that may be used in the study of electrolytes. The principal elements involved are in the form of the cations; $_{11}Na^{+}$, $_{12}Mg^{++}$, $_{19}K^{+}$, $_{20}Ca^{++}$; and the anions: $_{17}Cl^{-}$, $_{6}C$ as carbonate and bicarbonate, $_{15}P$ as the acid phosphates, and $_{16}S$ as sulfate—as well, of course, as $_{8}O$, which forms a part of all complex anions. Of these $_{8}O$ and $_{12}Mg^{++}$ do not, as already indicated, have useful radioactive species.

Of the main essential cations, $_{20}Ca$ and $_{12}Mg$ are also important bone minerals and organic metabolites. All of the elements involved in the essential anions, with the exception of $_{17}Cl$, also play a role in the intricate dynamics of intermediary metabolism. In addition phosphate and carbonate are, with $_{20}Ca$ and $_{12}Mg$, the principal constituents of bone. Therefore, of the elements occurring as electrolytes, it is $_{11}Na$, $_{19}K$, and $_{17}Cl$ that are of interest in metabolism largely because of their status as electrolytes. Most isotope research on the role of electrolytes has been done with isotopes of these three elements and our discussion here will be largely limited to them.

The use of isotopes provides the only method whereby the absolute values for the time of normal penetration and turnover of electrolytes in tissues and cell spaces can be determined. Much of the work so far has been directed toward elucidating these hitherto unsolvable problems.

Two papers of particular significance for the general study of ionic equilibria have been those of Hahn and Hevesy[45] and of Greenberg *et al.*[43] on the rate of penetration of ions through the capillary wall; the latter workers have in addition studied the permeability of the blood-cerebrospinal barrier to ions. Hahn and Hevesy[45] found with labeled chloride, bromide, $_{11}Na$, $_{19}K$, and phosphate ions injected into the circulation of rabbits, that potassium was by far the fastest to penetrate the capillary wall; from tissue measurements they also concluded that the capillary endothelium in muscle is much more permeable to $_{11}Na$ and phosphate than is the endothelium in the brain. Greenberg *et al.*[43] used labeled $_{11}Na$, $_{19}K$, phosphate, and iodide, which are normal to the body, and $_{37}Rb$, $_{38}Sr$, and bromide which they considered foreign. Disappearance of these ions from the plasma was in the order: $K^{+}=Rb^{+} >$ phosphate $> I^{-} > Na^{+} > = Br^{-} > Sr^{++}$. In the cerebrospinal fluid the increase in concentration followed the order: $K^{+} > Na^{+} > Br^{-} > Rb^{+} > Sr^{++} >$ phosphate $> I^{-}$.

Moore[99] has presented data on the determination of various fluid and tissue volumes of the human body with radioactive tracers of $_{11}Na$, $_{17}Cl$, and $_{19}K$, as well as with deuterium oxide.

Study of the uptake, distribution and excretion of $_{11}Na$ with the short-lived radioactive isotope, $_{11}Na^{24}$ (14.8 hour half-life) was first carried out by Hamilton and Stone[54] and by Hamilton[49]. In man, absorption of $_{11}Na$ taken by mouth was observed to begin within a few minutes and to be completed, in most cases, in between three and ten hours. In that period excretion was negligible.

Since this initial work there have been a number of studies on the movement of $_{11}Na$ across various body and cell membranes. Vischer *et al.*[146] have studied in detail the interchange between the $_{11}Na$

ion of the intestinal lumen and the blood and have concluded that the turnover between intestine and blood is very large, being equal to the total plasma $_{11}Na$ in approximately 83 minutes. Flexner and his associates have studied in several species the transfer of $_{11}Na$ across the placental barrier, including that of the human placenta (Gellhorn, Flexner, and Hellman[34]). In general, they have found that the transfer of $_{11}Na$ per unit weight of placenta increases greatly as gestation proceeds.

$_{11}Na$ is of particular interest as it is present predominantly as an extracellular cation. Manery and Bale[92], in rats and rabbits, and Kaltreider *et al.*[69], in man, have shown that within 9-12 hours complete equilibration of injected $_{11}Na$ is achieved, its spread from the plasma being rapid for the first two or three hours, and thereafter much slower. Kaltreider *et al.*[69] have given evidence for the view that the volume of fluid involved in the initial spread—averaging about 25 per cent of the body weight in man—represents the extracellular fluid volume.

Of particular clinical interest has been the study done with $_{11}Na^{24}$ by Fox and Keston[33] on the mechanism of shock from burns and trauma in mice. These workers have shown that the $_{11}Na$ content of injured skin is greatly increased, exceeding the gain in water (edema), and that under conditions of severe injury approximately one-half of the total amount of extracellular $_{11}Na$ is side-tracked and rendered unavailable to normal body interchange. They have concluded that the conventional extracellular fluid space has been modified into a much larger "sodium space" including extracellular edema fluid and intracellular water containing excess $_{11}Na$. Fox and Keston also noted a great influx of $_{11}Na$ into burned human tissues as determined by *in vivo* measurements at the bedside.

Some use of long-lived radiosodium—$_{11}Na^{22}$ (of 3.0 year half-life)—has also been made. Reaser and Burch[112] have used it in the study of the retention of $_{11}Na$ in congestive heart failure, and Cuthbertson and Greenberg[19] were able to demonstrate the increase of $_{11}Na$ space in the rat body under conditions of dietary chloride deficiency. This isotope should prove highly useful in many long-term studies of $_{11}Na$ turnover.

There is but a single useful isotope of radiopotassium—$_{19}K^{42}$ (of 12.4 hours half-life). It has been used in a number of studies on the uptake, distribution, and excretion of $_{19}K$. In contrast with $_{11}Na$, $_{19}K$ is present predominantly as an intracellular cation. Noonan *et al.*[105] have shown that, in rats injected with a labeled 1 per cent potassium chloride solution, $_{19}K$ ion penetrates rapidly into most tissues of the body, the rate being highest for liver, heart, kidney, lung, diaphragm, and gastrointestinal tract, intermediate for the general musculature and skin, and low for testes, erythrocytes, and brain. In tissues with rapid penetration, the total $_{19}K^{42}$ has a relative activity higher than the simultaneous plasma value during the first one to two hours; this is particularly marked after intraperitoneal injection. Fenn *et al.*[32], in a subsequent paper, verified these observations in the rabbit, cat, and dog. They concluded that an excess of $_{19}K$ in the plasma is quickly removed by the viscera, together with an anion, and is slowly released to the muscles.

Studies with radiochloride have been carried out thus far with one of the short-lived isotopes—$_{17}Cl^{38}$ (of 37 minute half-life). The long-lived species—$_{16}Cl^{36}$ (about 1,000,000 year half-life)—now available from the pile, may be expected to prove of considerable value. Manery and Haege[93] have studied the penetration of labeled chloride, administered as lithium chloride, into the tissues of the rat and rabbit. They have found that, after intravenous administration, equilibrium is reached within a few minutes in such organs and tissues as the kidney, liver, muscles, cartilage, and tendon, but that $_{17}Cl^{38}$ does not enter the entire chloride-containing phase of testes and pyloric mucosa even in one hour.

From the studies cited it can readily be seen that the use of tracers has a vital role to play in the elucidation of problems in electrolyte dynamics.

Bone metabolism. The most abundant elements in bone are $_{6}C$, $_{8}O$, $_{12}Mg$, $_{15}P$, and $_{21}Ca$. Of these only $_{20}Ca$ need be considered here, and with it $_{38}Sr$, which has been used as auxiliary label for $_{20}Ca$ by virtue of the metabolic similarity of these two elements and certain practical advantages of $_{38}Sr^{89}$ over $_{20}Ca^{45}$.

The single isotope of $_{20}Ca$ so far used is the unstable species $_{20}Ca^{45}$ (180 day half-life). It has been applied in several studies on the uptake of $_{20}Ca$ by osseous tissues. $_{20}Ca^{45}$ is stored almost entirely in bone (Pecher[108]; Greenberg[42]). Vitamin D has been shown to promote the absorption of $_{20}Ca$ from the digestive tract and the mineralization of the bones of rachitic rats.

$_{38}Sr^{85}$ (65 day half-life) has been used in a number of studies on bone metabolism. Upon injection $_{38}Sr$ rapidly concentrates in the skeleton, being at 24 hours about 100 times greater there per unit weight than in the soft tissues (Pecher[108]). Studies on bone fracture healing (Copp and Greenberg[18]) have shown that recalcification, as judged by $_{38}Sr^{85}$ uptake, is less active in vitamin A and D deficient and D hypervitaminotic rats than in normal rats.

Studies on the Essential Trace Elements:

Introduction. The best known trace elements in mammalian physiology are $_{26}Fe$ and $_{53}I$. $_{25}Mn$ and $_{29}Cu$ are also known to be essential; and evidence for $_{27}Co$ and particularly $_{30}Zn$ is almost conclusive. Some evidence also exists that $_{35}Br$ and possibly $_{28}Ni$ may be essential micronutrilites. Although fluorine ($_{9}F$) is known to aid resistance to dental caries, there is no evidence as yet that it plays an essential role. Considerable amounts of silicon ($_{14}Si$) and aluminum ($_{13}Al$) occur in the vertebrate body, but no requirements have been demonstrated for these elements.

Of the essential trace elements only $_{26}Fe$ and $_{53}I$ have been extensively studied with tracers.

Iron. Two radioactive species of $_{26}Fe$—$_{26}Fe^{55}$ ($\sim$ 4 year half-life) and $_{26}Fe^{59}$ (47 day half-life) have been used in tracer experiments. $_{26}Fe$ metabolism.

particularly as studied with tracers, has recently been reviewed by Hahn.[46]

Of particular medical interest has been work on blood preservation as studied with both $_{26}$Fe isotopes. Gibson *et al*[35, 36] have done extensive studies on the use of various preservatives in relation to the survival of transfused cells after *in vitro* storage. They have found that refrigeration, the addition of dextrose to the citrate anticoagulant, the maintenance of a slightly acid reaction of the diluted plasma or resuspension fluid, and optimal dilution are essential for prolonged preservation. In certain acid-citrate solutions whole blood can be safely preserved with up to 70 per cent viability for three weeks. Cells preserved by the simple addition of citrate are almost entirely broken down within 24 hours in the new host after only two weeks of preservation *in vitro*, as first shown with radioiron by Ross and Chapin[116]. Other significant studies have been the determination of red cell and plasma distribution and volume with radioiron-labeled erythrocytes by Gibson *et al.*[37-39] and the demonstration by Moore *et al.*[98] and Hahn *et al.*[47] that ferrous $_{26}$Fe is better absorbed from the gastrointestinal tract than ferric $_{26}$Fe.

Iodine. Three $_{53}$I species, all radioactive, have been used in tracer studies—$_{53}I^{128}$ (24.99 minute half-life), $_{53}I^{130}$ (12.6 hour half-life), and $_{53}I^{131}$ (8 day half-life). Most work at present is being done with the last of these. $_{53}$I metabolism in the mammal, particularly as studied with tracers, has recently been reviewed by Leblond[84].

The $_{53}$I label has permitted the solution of many vital problems relating to the physiology of the thyroid gland. Before radioiodine became available, the entrance of $_{53}$I into the gland could not be studied under physiological conditions. When minute doses are administered to the mammal, a high proportion becomes incorporated into the gland—about 60 per cent in the rat by 24 hours and about 50 per cent in man. Among the many other important problems of thyroid physiology that have been solved may also be mentioned the recent demonstration by Taurog and Chaikoff[138] that the circulating hormone in the plasma is almost certainly thyroxine.

Reiner *et al.*[114] have been able to study the absorption rates of insulin labeled by coupling it with diazotized iodoniline containing radioiodine. A correlation was found between the differences in absorption rate and the intensity of hypoglycemic action produced. In the preparation used, absorption was found to be in the following order: insulin > globin insulin (with zinc) > protamine zinc insulin.

Other trace elements. Few studies have been carried out with isotopes of $_{25}$Mn, $_{27}$Co, $_{29}$Cu, and $_{30}$Zn. Representative studies are cited in Table 1. Some studies using radioactive $_{35}$Br have already been mentioned under the discussion of electrolytes. Also worthy of special note is the demonstration with $_{35}Br^{82}$ (34 hour half-life) that bromine is concentrated in the thyroid (Perlman, Morton, and Chaikoff[109]).

Studies on Elements Not Known to be Essential in Mammalian Nutrition:

At least 78 elements are not known or believed to be directly essential for mammals, although the need of various plants for other elements, especially boron ($_5$B) and molybdenum ($_{42}$Mo), has been conclusively demonstrated, also the need of certain lower animals for such elements as vanadium ($_{24}$V), silicon ($_{14}$Si), etc. A minority of these 78 elements has been studied in mammals with isotopic tracers—in connection with their behavior when present either in trace or toxicological amounts. It is interesting to speculate as to how many elements will eventually be found to be essential in trace amounts.

For over 45 years there has been interest in the biological effects of the naturally occurring radioactive elements, particularly $_{88}$Ra, $_{90}$Th, and $_{92}$U. In the case of $_{88}$Ra in particular, there have been many studies on its distribution after injection or ingestion in mammals; assays for the contents of these elements in tissues have, in most cases, been made with various techniques of measurement for radioactivity. The literature on $_{88}$Ra and $_{92}$U up to 1933 has been reviewed in detail in the book by Stoklasa and Penkava[131]. However, the main emphasis of these studies has been investigation of the toxic and radiation effects of the heavy radioactive elements rather than tracing their fate in the body. One important fact deriving from these studies has been that $_{88}$Ra, like many of the heavy metals, is deposited in bone and, by its chronic radiation effects, there may induce malignant change (cf. Lisco *et al.*[86], in the case of $_{38}$Sr and $_{94}$Pu). These effects are reviewed by Stoklasa and Penkava.

Recently there has been considerable interest in the fate *in vivo* of trace amounts of elements now thought to be nonessential or foreign to the mamalian body. In such experiments the amount of the labeled element introduced should be so small as to have no manifest toxic or pharmacological effect and no detectable radiation effect on the organism as a whole. So far 29 nonessential elements have been studied on this basis: beryllium ($_4$Be), fluorine ($_9$F), argon ($_{18}$A), arsenic ($_{33}$As), selenium ($_{34}$Se), krypton ($_{36}$Kr), rubidium ($_{37}$Rb), strontium ($_{38}$Sr), yttrium ($_{39}$Y), zirconium ($_{40}$Zr), columbium ($_{41}$Cb), molybdenum ($_{42}$Mo), ruthenium ($_{44}$Ru), antimony ($_{51}$Sb), tellurium ($_{52}$Te), xenon ($_{54}$Xe), cesium ($_{55}$Cs), barium ($_{56}$Ba), lanthanum ($_{57}$La), cerium ($_{58}$Ce), praseodymium ($_{59}$Pr), element 61, gold ($_{79}$A), lead ($_{82}$Pb), bismuth ($_{83}$Bi), astatine ($_{85}$At), radon ($_{86}$Rn), thorium ($_{90}$Th), protoactinium ($_{91}$Pa), neptunium ($_{93}$Np), plutonium ($_{94}$Pu), americium ($_{95}$Am), and curium ($_{96}$Cm). Citations for these studies are included in Table 1 under the respective elements.

Certain of the foregoing studies have particular medical significance. Hamilton[50] who has studied the distribution in rats of a large number of the above elements administered in trace amounts, has demonstrated with radioisotopes the selective localization of many in bone—particularly of $_{39}$Y and $_{58}$Ce (fission products) and $_{94}Pu^{239}$ (a product of $_{92}U^{238}$

neutron capture); these elements are excreted very slowly and have biological half-lives in the body of from one to three years. Since they are long-lived species and are abundantly produced in the pile, they constitute a potential health hazard for the personnel of atomic energy installations.

The use of radioisotopes has been of considerable value in showing the distribution of nonessential elements used in pharmacology. For example, Bertrand and Tobias[7] have demonstrated with radiogold that the uptake of gold sodium thiosulfate in the synovia and synovial fluid of a patient suffering from rheumatoid arthritis, and of rabbits in which chemical (turpentine) arthritis has been induced, was very marked, while, in the case of control animals, uptake was somewhat less. Such studies are of value in relation to the use of $_{79}Au$ salts in rheumatoid arthritis. The use of radioantimony—$_{51}Sb^{124}$—by Brady *et al.*[11] in the study of *Dirofilaria immitis* infection (filariasis) in dogs, has shown that sodium antimony xylitol is taken up in significant amounts by the adult worms, which concentrate it only less than the thyroid and liver. Similar studies with radioarsenic—$_{33}As^{74}$—by Lawton *et al.*[83] on *Litosomoides carinii* infection (filariasis) of the cotton rat, have shown the concentrating of sodium arsenite by the parasites. Such studies can be expected to aid in our understanding of the mechanism of many pharmacological agents and may possibly point the way toward the development of new techniques.

$_{35}Br$, an element that possibly plays an essential role in animal nutrition, has been used in radioactive form to label a number of dyes. For example, Moore and Tobin[100] have been able to show by this means the selective localization of labeled and dibrom trypan blue in inflammatory lesions.

In summary, it may be noted that, in the application of radioactive isotopes of the majority of elements to biological problems, we are still in a primitive stage. Before the wide adoption of these new techniques a new generation of workers must be trained. The field has just opened up, and the future will see much further work and many important discoveries.

The list of references for this article appeared at the end of Part I which was printed in the July issue of California Medicine.

California Cancer Commission Studies*

Chapter XXI

Cancer of the Anus, Rectum and Rectosigmoid

William H. Daniel, M.D., *Los Angeles*

THIS chapter will be limited, insofar as anatomical boundaries and symptoms permit, to discussion of cancer of the anus, rectum and rectosigmoid. The rectosigmoid has no definite landmarks, but will be considered to comprise that portion of the bowel above the ampulla of the rectum and below the movable portion of the sigmoid, the upper part lying at and just above the pelvic peritoneal reflection.

INCIDENCE

According to the Bureau of Vital Statistics, cancer of this area is ranked number four in frequency among all cancers of the body. In 1890 there were two deaths per 100,000 population reported as caused by cancer of the anus, rectum and rectosigmoid, and in 1940 6.7 deaths per 100,000 were reported from this cause. This apparent increase, however, may be accounted for, in part at least, by better clinical and postmortem diagnosis.

The majority of patients with this disease are between 50 and 75 years of age, but 20 per cent are under 50. About 3 per cent of cancers in this area of the body occur in patients between the ages of 20 and 30. It is in this decade of life that they are most often overlooked and for this reason are either inoperable or incurable when the diagnosis is made. There is no "cancer age."

DIAGNOSIS

There are few early signs or symptoms. Symptoms commonly related by patients are change in bowel function (especially frequency, which is too often called diarrhea, or dysentery) with an unsatisfied desire to stool; the passage of blood and mucus; abdominal discomfort; loss of appetite; nausea and vomiting. Pain is not marked except in anal lesions.

Often the patient reports rectal bleeding, and this should never be attributed to hemorrhoids without a digital, proctoscopic examination and roentgen studies to rule out the presence of more serious lesions higher in the bowel.

Proper palpation of the rectum with the patient in the lateral position will reveal 80 per cent of the lesions in this area. The lesion may be a polyp, with a pedunculated or sessile base, a broad flat soft villous adenoma, a polypoid mass, a craterlike ulcer with hard margins or an annular lesion involving all surfaces of the bowel. (See Figure 1.) By use of the sigmoidoscope these lesions can be visualized.

Cancer at the anal opening may resemble a chronic anal ulcer with an indurated base, and may originate in the perianal and perirectal glands as an adenocarcinoma, or from the anal integument as an epithelioma (epidermoid carcinoma). (See Figure 2.) The epithelioma may metastasize to the inguinal nodes, as well as spread upward in the perirectal spaces.

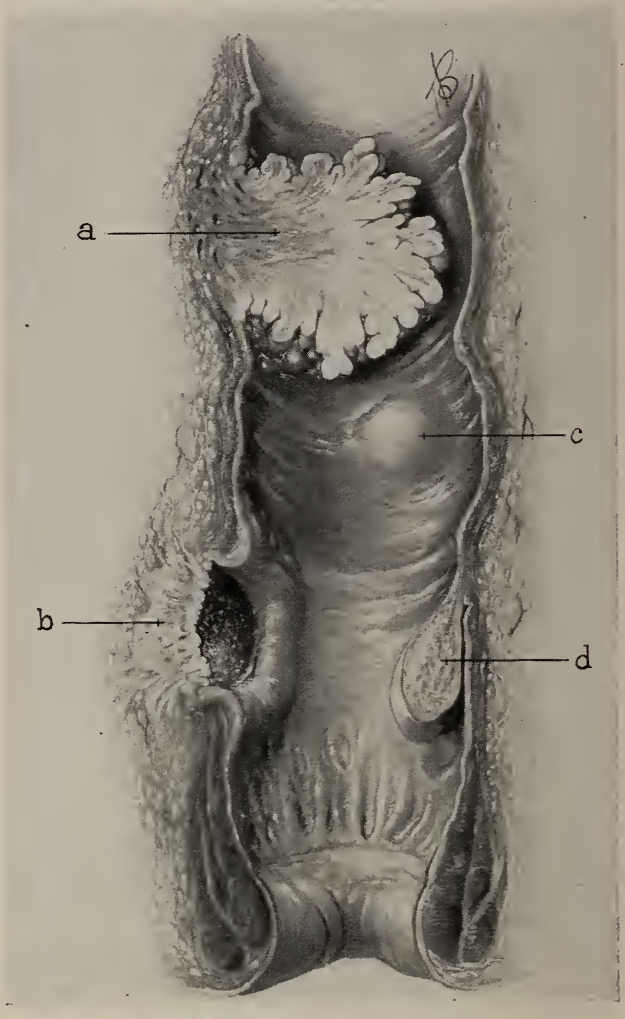


Figure 1. Drawing illustrating: (a) Polypoid carcinoma with moderate involvement of the bowel wall, (b) Ulcerating carcinoma with marked penetration of bowel wall and with rolled up edges, (c) Adenoma which may become a polyp or a cancer, (d) Benign polyp on short pedicle. The mucus membrane is normal.

All suspicious lesions should be biopsied. If the first specimen is negative the biopsy should be repeated. Sigmoidoscopic examination should be done under intravenous anesthesia if the instrument cannot be passed to eight inches, especially if bleeding is a constant symptom. Negative findings in a roentgen examination with barium enema are not conclusive in the lower eight inches of the colon and may be dangerously misleading because a filling defect is usually obscured by other loops of bowel. A barium enema should never be given preceding the sigmoidoscopic examination. When given at any time it

*Organized by the Editorial Committee of the California Cancer Commission.

should be done with caution lest a partial obstruction be made total.

Pathologists differ widely in the diagnosis of adenomas and polyps. Many classify them as Grade I carcinomas, whereas others will call the same lesions benign. (Figure 3.) These lesions should always be regarded at least as premalignant.

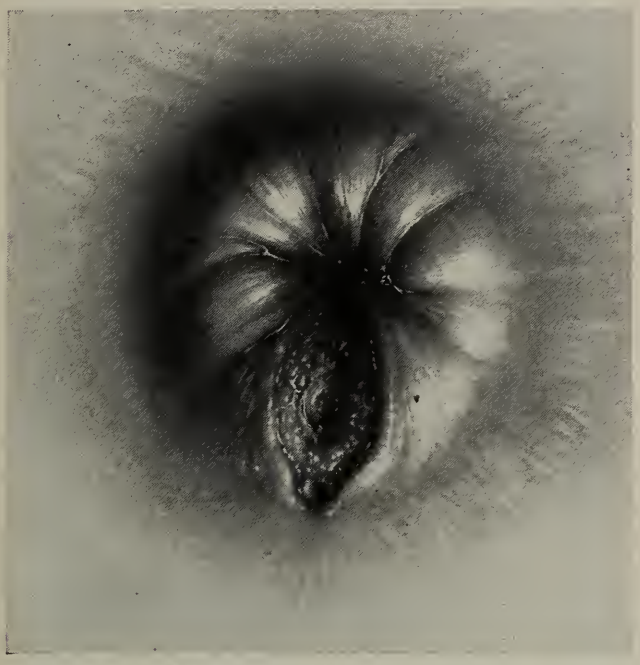


Figure 2. Anal epithelioma, or epidermoid carcinoma. Shows ulceration of anal integument involving deep structures. May resemble other anal ulcerative lesions.

The grading of frank adenocarcinomas should not influence the treatment; whatever the grade, radical removal is indicated. (Figure 4.)

Differential diagnosis must be made from sarcomas (rare), metastases from upper abdominal lesions (stomach, pancreas, ovary, uterus, bladder, colon), prostatic disease, from ulcers due to X-ray or radium therapy, from chronic infection such as amebic granulomas, lymphogranuloma inguinale, chronic ulcerative colitis, ordinary chronic anal fissures and tuberculosis and luetic ulcers. Biopsies are necessary to rule out carcinoma.

TREATMENT

The patient is entitled to every means for a cure and should not be denied an exploratory procedure unless the case is utterly hopeless. The object of treatment is to cure the cancer or prolong life for a maximum period with a minimum of disability and discomfort. The patient should be informed of the seriousness of his condition and that his cooperation is essential for recovery. The patient who is a poor surgical risk should be built up generally so that he can stand the radical procedure. Occasionally it may be necessary to do the operations in two stages.

Operability and curability must be determined by



Figure 3. Adenoma of rectum (x 65) normal glandular epithelium at left. To right adenomatous epithelium exhibiting slight hyperchromatism of nuclei and almost perfect polarity but producing larger imperfectly shaped glands.

an evaluation of all the factors concerned, such as age and general condition of patient, type, size and location of growth, and the presence of metastases. Small movable tumors are often more likely to spread earlier than those which have become surrounded by inflammatory tissue. A tumor which may be resectable may be inoperable because of the poor general condition of the patient. Curability can be estimated only in the absence of demonstrable metastases.

Cure of cancer of the rectum involves many factors. Cancer cells infiltrate locally and spread to remote areas by way of lymphatics and veins, therefore the most radical removal of the growth with the structures which transmit these cells is essential, even though it entails complex changes in the anatomy of the individual. The surgeon should be competent to perform all accepted procedures, and should be capable of planning and carrying out the operation best suited to the individual patient.

A number of surgical procedures require a permanent abdominal colostomy. To obviate the necessity of the abdominal artificial anus (which the patient and his medical advisors are still somewhat loath to accept because of the unfounded stigma attached to it or because they have not been trained in its management), many procedures have been tried and many found inadequate or undesirable. An uncontrollable perineal anus has been proven less practical than one in the abdomen, which can be managed with much less effort. The objections to an abdominal anus are unfounded. A properly constructed colostomy, irrigated thoroughly every other day will not be odorous nor will it soil the patient's clothing.

ABDOMINOPERINEAL RESECTION

The present consensus is that the combined abdominoperineal resection of the rectum and rectosigmoid with a permanent abdominal colostomy offers the best chance of cure in the majority of cases. The one-stage procedure is the method of choice in good risks. For those in whom medical decompression of an obstructed colon has not been successful, a cecostomy or transverse colostomy should be done and this followed in a short time by the combined abdominoperineal resection. (Figure 5.)

COLOSTOMY AND POSTERIOR RESECTION

Another method, the colostomy and posterior resection, is suitable for removal of low growths in



Figure 4. Adenocarcinoma of rectum (x 75) grade II malignancy. Normal glandular tissue at upper left. Tumor tissue at right exhibits very irregular glands made up of cells exhibiting marked hyperchromatism, occasional abnormal mitoses and loss of polarity. The stroma is considerably infiltrated by leukocytes.

certain patients who are *poor surgical risks* because of cardio-circulatory-renal impairment or in patients who are at an age at which the expectancy of life is limited. The amount of the bowel and lymphatic structures removed is not as great as the amount removed in the abdominoperineal procedure.

COLOSTOMY AND ANTERIOR RESECTION

High rectal and rectosigmoid growths, in the presence of metastases, may be removed by anterior resection, the lower rectal stump being left *in situ*. A permanent abdominal colostomy is established.

ANTERIOR RESECTION WITH END-TO-END ANASTOMOSIS

Several surgeons have advocated and performed resections of lesions in the rectosigmoid and upper rectum with reestablishment of continuity of the bowel, with or without complementary temporary colostomy. This would be the ideal procedure if it did not jeopardize the chance of cure by failing to remove all the cancer-carrying elements. Several techniques for this operation have been described, the merits of which cannot be determined without the test of time. Constriction of the anastomotic site is one of the disadvantages of this procedure.

PROCTOSIGMOIDECTOMY WITH PRESERVATION OF ANAL SPHINCTERS

Abdominoperineal resection without abdominal colostomy and with preservation of the anal sphincter (so-called "pull-through operation") is the method of choice with some surgeons in selected cases. The lesion must be far enough above the anus (2 or 3 inches) to insure removal of downward lymphatic spread, and the length of the viable sigmoid must be adequate to reach well beyond the anal outlet. There is considerable controversy concerning the degree of bowel control following this procedure.

Anal epitheliomas (Figure 6) are treated by radical surgical removal (abdominoperineal resection) followed by block dissection of both inguinal regions.

A curative, and also a preventative, procedure is the destruction of all adenomas, polyps and papillomas by cauterization or desiccation. Removal of all such lesions is essential in the preventative program.

Other methods of treatment—local excision, colostomy and perineal excision, cauterization, fulguration and irradiation—should be considered as palliative and not curative. Colostomy relieves obstruction only. The removal of the primary lesion, even in the incurable, affords a comfort to body and mind that is worth the hazard and effort.

MANAGEMENT

Success depends upon a correlation of all clinical tests: complete blood examination; blood chemistry determinations; estimation of nonprotein nitrogen; determination of prothrombin level; serum albumin and liver function tests when liver damage is suspected. The internist or cardiologist should interpret the electrocardiogram tracings and physical findings in terms of surgical risk. It is essential to have an x-ray film of the chest. Finding of a small or moderate metastasis does not contraindicate removal of



Figure 5. Photograph of excised rectum with annular ulcerating nodular lesion involving the mid-portion.

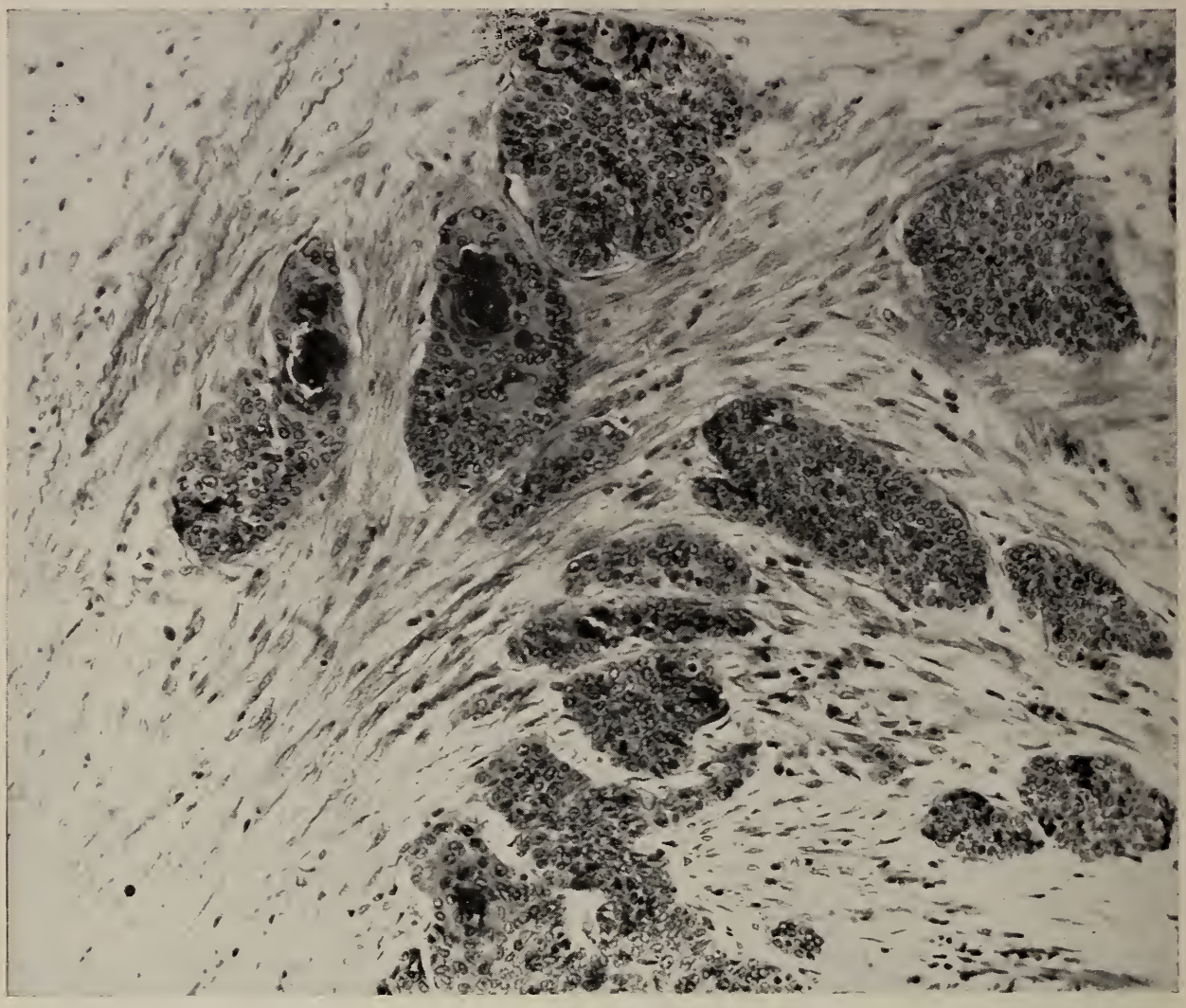


Figure 6. Epidermoid carcinoma of anus (x 70). There is no normal tissue present for comparison. The lesion is composed of irregular masses of squamous cells in the centers of some of which are masses of keratin, "epithelial pearls" (black in photograph).

the primary lesion. Cystoscopic study of the bladder, ureters and kidneys is essential in the presence of growths which may involve these organs. Vitamin deficiencies must be corrected, and anemia, which is a common finding, must be overcome by repeated transfusions of whole blood.

The bowel must be decompressed by saline irrigations, mineral oil and castor oil. A sulfa drug (sulfasuxidine at present is most favored) is given in appropriate doses for approximately one week before operation. This is essential in those cases in which a resection and anastomosis is contemplated. Thorough decompression is of paramount importance in all cases because the handling of a distended bowel predisposes to peritonitis with all its sequelae, especially small bowel obstruction.

Postoperative care entails a careful watch for and prompt treatment of such complications as shock, atelectasis, hemorrhage, circulatory collapse, phlebitis, obstruction, peritonitis and embolism. When whole blood is not available to combat shock, plasma and washed red cells are valuable.

SUMMARY

1. There is no "cancer age."
2. Any abnormal manifestation of bowel function should be considered to be the result of onset of cancer until cancer is disproved.
3. Routine thorough rectal palpation and instrumental examination are essential.
4. X-ray examination, especially with barium enema, should never be carried out prior to a sigmoidoscopic examination when cancer of the rectum is suspected.
5. The surgical procedure should be selected for each individual.
6. The growth should be removed whenever possible.
7. Proper preoperative and postoperative management is essential in decreasing morbidity and mortality.

"Cancer of the Liver, Gallbladder, and Extrahepatic Ducts, and Pancreas" by William F. Rowe, M.D., and E. Eric Larson, M.D., Chapter XXII of the California Cancer Commission Studies, will appear in this section in the September issue of CALIFORNIA MEDICINE.

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For Information on Preparation of Manuscript, See Advertising Page 2

EDITORIALS

Hospitals in Practice

Of tremendous interest to all physicians, and of specific interest to those who practice as salaried employees of hospitals, is the opinion rendered last May 19 by the office of the Attorney General of the State of California.* This opinion, given in response to a request by the State Board of Medical Examiners, holds in no uncertain language that a non-profit hospital is not permitted by law to engage in the practice of medicine and that the employment of physicians on a salary basis, with the hospital billing and collecting from the patients, is an illegal act which is specifically prohibited by law.

The case in point arises from an inquiry from a non-profit hospital association which sought this opinion before proceeding to employ a pathologist on a salary basis. The opinion leaves no room for doubt that such employment constitutes the practice of medicine and that such practice is illegal, whether performed directly or indirectly. It also reemphasizes earlier court decisions to the effect that the practice of pathology is a diagnostic procedure which is as much a part of the practice of medicine as the giving of remedies.

The California Medical Association has long held that the practice of medicine by hospitals, particularly through the employment of pathologists, radiologists and anesthesiologists, is a violation of both ethical and legal requirements. Nevertheless, many hospitals have found such practices to be financially profitable and have extended such employment to the furthest possible point. It now appears that such hospitals will have to reevaluate their individual positions and make new arrangements with the professional men practising within the hospital properties. The Association has long contended that there is no essential difference between the employment of pathologists on a salary basis by such hospitals and the employment of obstetricians, surgeons or other physicians who confine their activities to one specialty. The opinion of the Attorney General's office bears out this conclusion in every detail and should do much to clear up a growing tendency to exploit physicians.

The medical profession in California has gained immeasurably by this opinion in its effort to keep the practice of medicine a free enterprise, not under the domination or control of outside groups or interests, either private or governmental. The Hon. Fred N. Howser, California's able Attorney General, is to be commended on his sincerity, forthrightness and courage in issuing this opinion in the interests of sound professional practice.

*This opinion will be found in full on p. 172 of this issue.

What Is the C.M.A.?

From time to time some members of the California Medical Association propound the above or similar questions, seeking to learn just what it is that the Association does in return for the dues paid by the members. This has been particularly true in recent years, when the dues have been at a higher level than in prewar years.

From time to time various answers to this question have been formulated and distributed. The answers were not always the same but in general they followed the same pattern and hit the same high spots.

Now, in response to an inquiry by the Collector of Internal Revenue, the Association has again digested its activities. Once more some concentrated thought has been put into this subject and an up-to-date answer given to the recurring question.

To those members who may have asked or thought of this question, even though not asking it, the digest of C.M.A. activities appearing on page 161 of this issue should be of interest. To other members who may not have had this question cross their minds, a review of C.M.A. activities is still a good project. A few minutes spent on this digest, a little thought given to the subject matter covered, would be a good investment in recommended reading.

Letters to the Editor . . .

Santa Monica

The Editor
CALIFORNIA MEDICINE

Dear Sir:

In the May issue of CALIFORNIA MEDICINE appears an article entitled "A Therapy of Proved Efficacy in Otomycosis" by Ben L. Bryant of Los Angeles. The remarkable thing about this article is the fact that a series of cases is reported as "otomycosis" without the slightest reference to how that diagnosis was established in any of the cases. Reference is made to a similar condition in which bacteriological examination showed among other things, "numerous unidentified large gram positive bacilli, frequently occurring in chains"; this was not to be confused with "otomycosis." It was further pointed out that the treatment suggested was not successful in combatting infection with *Aspergillus Niger* (the best recognized form of otomycosis). In view of the remarks made regarding these conditions, it appears that some bacteriologic or mycologic studies were made, but the author makes no mention of the results of such studies in the cases which he considered to be otomycosis about which the article is written and for which his treatment is effective.

Dermatologists in general are likely to be confused by the otologist's diagnosis of otomycosis, and this article serves to compound the confusion further. What type of otomycosis other than that due to *Aspergillus Niger* is recognized by otologists, what is the identity of the mycotic invader at fault and how is the diagnosis made? Perhaps it is diagnosed by "therapeutic test" with the "therapy of proved efficacy" suggested in the article to which I refer.

Yours very truly,

A. FLETCHER HALL, M.D.

This letter was forwarded to Dr. Bryant, whose reply appears in the adjoining column.

Editor, Los Angeles
CALIFORNIA MEDICINE

Dear Sir:

I have read the letter addressed to you by Dr. A. Fletcher Hall regarding my article, "A Therapy of Proved Efficacy in Otomycosis," which appeared in the May issue of CALIFORNIA MEDICINE.

In reply to Dr. Hall's statement that there was no reference in the article as to how the diagnosis was established, I refer him to the first paragraph of that portion of the paper headed, "Therapy of Otomycosis," and particularly to the last sentence of this paragraph, namely: "The appearance of the canal is so characteristic that, after some experience, it is unnecessary to make routine microscopical examinations, particularly since the fact that the treatment is universally effective obviates the necessity of identification of the various mycotic strains." I abide by this statement. Certainly, at the outset of this study routine microscopic examinations were made and revealed the various mycelial strains found in otomycosis. I certainly disagree with Dr. Hall's statement that infection with *Aspergillus Niger* is the best recognized form of otomycosis, and I feel that this subject is dealt with sufficiently in the paper.

As cases of this type were seen over and over again, it became necessary to make microscopical studies only in those cases which presented some unusual clinical feature, and I feel that this practice is not too different from that followed in general or dermatological work.

I regret exceedingly that my article "serves to compound the confusion further" for Dr. Hall. I can only say that the facts presented and the treatment outlined have served to clarify this problem for many otologists and general practitioners. The series of cases presented has been augmented by several hundred additional cases, the outcome of which has served to support the statements made.

Yours very truly,

BEN L. BRYANT

CALIFORNIA MEDICAL ASSOCIATION

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R. STANLEY KNEESHAW.....President-Elect
LEWIS A. ALESEN, M.D.....Speaker
DONALD A. CHARNOCK, M.D.....Vice-Speaker
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SIDNEY J. SHIPMAN, M.D.....Chairman, Executive Committee
DWIGHT L. WILBUR, M.D.....Editor
JOHN HUNTON.....Executive Secretary

NOTICES AND REPORTS

Your Medical Association

In reply to a request by the Commissioner of Internal Revenue for information needed for a review of the tax-exempt status of the California Medical Association, the association's legal counsel has prepared and sent to the commissioner the following statement of the organization's purposes and activities.

1. STATEMENT OF ACTIVITIES

Executive Offices:

Executive offices of the Association are maintained at 450 Sutter Street, San Francisco, California, and 606 Subway Terminal Building, 417 South Hill Street, Los Angeles, California, for the purpose of administering and coordinating the activities of the Association and editing and compiling the monthly scientific publication of the Association known as CALIFORNIA MEDICINE. A full-time staff is employed, composed of: The Executive Secretary, Field Secretary, Assistant Executive Secretary, Editorial Assistant, Advertising Manager and five stenographers and clerks. The Editor of CALIFORNIA MEDICINE is a physician employed on a part-time basis to supervise the editing and publishing of the magazine. The Executive Secretary serves as business manager of the magazine. The amounts paid to employees of the Association during 1946 and 1947 are set forth in the statements of receipts and disbursements for said years that are attached hereto and made a part of this affidavit.

The policies which guide the executive and administrative staff are laid down by the House of Delegates of the Association, composed of slightly over two hundred physicians who are elected by their respective county medical societies; by the Council of the Association, which is the executive body and is composed of fifteen councilors plus the officers of the Association, all of whom are elected by the House of Delegates; and the officers of the Association, consisting of the president, president elect, speaker, vice speaker, and secretary-treasurer. All delegates, councilors and officers of the Association are physicians.

California Medicine:

One of the prime activities of the California Medical Association is to carry on a program of education for the benefit of its members, at present approximately nine thousand four hundred doctors of medicine in the State of California. CALIFORNIA MEDICINE constitutes one of the chief media used by the Association to carry out this purpose. Each issue contains articles on scientific medicine, clinical medicine, medical research, and public health, together with news articles of interest to the medical profession and comments and editorials on the scientific, social and economic aspects of the practice of medicine. Copies are furnished all members without additional charge and as a part of their membership benefits. It is printed by a private printing firm, under contract with the Association. Most of the articles appearing in it are prepared by members of the Association or by physicians from other states. Copy is prepared or edited in the executive offices, where proof is read, mailing envelopes are addressed, and all circulation and advertising matters are handled. CALIFORNIA MEDICINE is not a profit-making project, as revenue derived from advertising has often covered only a portion of the cost of publication.

CALIFORNIA MEDICINE is published monthly, and representative copies of it are submitted herewith in accordance with the request contained in your letter of June 7, 1948.

Cancer Commission:

The Association maintains a Cancer Commission, composed of nine physicians who are members of the Association. It is the function of the Cancer Commission, which it has diligently carried out during the years in question, to stimulate and aid in the education of the public toward the understanding of cancer, to promote research leading toward development of means of alleviating or curing cancer, and to promote and stimulate dissemination of knowledge amongst practicing physicians with respect to methods and procedures for detecting and diagnosing cancer and treatment of same. The Cancer Commission of the California Medical Association has joined with the American Cancer Society and formed a California nonprofit charitable corporation, known as the American Cancer Society, California Division.

This corporation, managed jointly by the Cancer Commission of the California Medical Association and public-spirited citizens, commenced in 1945 an active campaign in California,

(a) To educate the public to recognize symptoms that might indicate the presence of cancer and to seek early medical attention when such symptoms arise,

(b) To stimulate and aid and assist in the establishment of consultative tumor boards, conducted without charge to the public,

(c) To aid and assist in the care and treatment of needy persons having cancer.

(d) To promote, aid and assist research in the field of cancer.

Prior to January, 1946, the Cancer Commission did not employ any full-time assistants. Since then, however, it has employed a physician as its medical director on a full-time basis. The medical director of the Cancer Commission also serves as medical director of the American Cancer Society, California Division, and his salary, costs and expenses are shared by this Association and the American Cancer Society, California Division.

Postgraduate Study:

The Association, through its standing committee on postgraduate activities, maintains throughout California an active program of postgraduate education of its members. Prior to 1947, the committee on postgraduate activities functioned through the employees in the executive offices. However, in 1947 a physician member of this Association was employed on a part-time basis to act as director of postgraduate activities, and in the latter part of 1947 a contract was entered into under which the duties of the director of postgraduate activities will become a full-time function. Conferences and meetings for postgraduate study have been arranged in various parts of California, and this work of the Association is carried on continuously.

Physicians Benevolences:

For the purpose of providing aid to aged physicians who are in financial need and to the families of members or former members of the Association who are in need, the Association maintains a committee on physicians benevolences. By action of the House of Delegates of the Association the sum of $1 per member is irrevocably set aside each year out of the revenues of the Association for the physicians benevolences fund. This fund is used only for the purpose of granting financial assistance to needy physicians or to the families of needy physicians.

Blood Bank Activities:

The Association maintains a special committee on blood banks. This committee during the years 1945, 1946 and 1947 has cooperated and coordinated with the blood bank advisory committee of the California State Department of Public Health, and with blood banks maintained by several of the component county medical societies in California. The work of the blood bank committee has involved aid and assistance in the entire field of collection, processing, and distribution of blood and blood plasma.

Public Relations:

As a part of its purposes, viz. to promote the science and art of medicine and to protect the public health, the Association during 1945, 1946 and 1947 carried on an active public relations program under the direction of its Council and Executive Committee. The purpose of this program was to acquaint the public with medical and public health facts, and to enlist the cooperation of the public in activities designed to maintain and improve the health of all citizens. Particularly, a public educational campaign was carried on to point out the benefits to the public of enrolling in accredited, approved and reputable health insurance programs. The public relations activities of the Association have been carried on in the following ways:

(a) Through the promotion in each community in California of a "voluntary health week" proclaimed by the mayor of the community, during which public meetings were arranged and speakers obtained for the purpose of acquainting the citizens of the community with the availability of voluntary health insurance plans and the desirability of protecting against the costs of medical care by purchasing health insurance contracts. There are fifty-eight counties in California, and during the years 1946 and 1947 voluntary health weeks were held in most of the counties. The Association maintained a special staff for the purpose of arranging and organizing voluntary health weeks, and this staff devoted its full time during the years 1946 and 1947 to the conduct of public health weeks.

(b) Through supplying speakers for meetings of lay groups and organizations on public health and medical subjects.

(c) Through a radio program sponsored by the Association, established in May, 1946 through the Mutual Broadcasting System, and in 1947 transferred to the American Broadcasting System. This radio program is entitled "California Caravan" and is a weekly program. Each week a historical drama portraying a significant historical event in California is presented, together with a statement on behalf of the Association advocating in the public interest that voluntary health insurance be obtained by California families. While the program does not limit itself to any one health insurance plan, emphasis is placed on California Physicians' Service, nonprofit California corporation in which almost all of the members of the Association are members and which on a nonprofit service basis offers medical, surgical and hospital care to the public on a prepayment basis (for the status of California Physicians' Service, see *California Physicians' Service v. Garrison, 28* Cal. (2d) 790).

(d) Through newspaper releases on medical and health subjects.

(e) Through conferences and personal contacts with representatives of many organizations and groups.

Public Policy and Legislation:

The standing committee on public policy and legislation of the Association reviews legislative proposals pending in the California Legislature, analyzes these proposals, and through the publications of the Association and correspondence acquaints the individual members of the Association with the nature of such legislative proposals. Members of this committee and the officers of the Association supply members of the State Legislature with information on medical and health questions, and appear before committees of the Legislature and express the views and policies of the medical profession of California on pending legislative matters.

With respect to national legislative proposals affecting medicine and the public health, this Association does not carry on any direct activity. However, through its committee on public policy and legislation it maintains membership in The United Public Health League, a nonprofit association of medical societies and doctors of medicine in the eleven western states. The United Public Health League fulfills essentially the same functions with respect to the Congress that the committee on public policy and legislation of this Association fulfills with respect to the California Legislature.

Hospital Construction:

During the past several years there has been a shortage of hospital beds in California, and through state and federal legislation the California State Department of Public Health has been designated as the state agency, having charge of new hospital construction, and has federal and state grants to dispense to new hospital projects. Officers and employees of the Association have served on advisory committees with the State Department of Public Health, on special committees of the State Chamber of Commerce, and the Association itself, through its executive officers, has acted as a clearing house for information concerning new hospital construction. The activities of the Association in this field have consumed a great deal of time of the officers and employees of the Association, and have had as their object and purpose the correlation and promotion of needed hospital construction in this state.

Placing Physicians:

The Association maintains a placement service for physicians seeking locations in California and for physicians, hospitals, communities or others seeking medical services. This service is provided without charge to either the physician seeking placement or those seeking medical services. It is of particular use and advantage to small rural communities where the provision of medical care is more of a problem because of greater distances, sparser population and inferior equipment available to the practicing physician. This service is available to all physicians, regardless of their membership status in the Association, and to all communities, civic organizations, hospitals or others. It functions throughout the year and has been successful in placing numerous physicians in areas where their services are of benefit to the community and the public health.

Industrial Practice:

Through the standing committee on industrial practice and the executive officers of the Association, the Association has cooperated with the State Industrial Accident Commission in the establishment and maintenance of minimum fee schedules for physicians performing services that fall within the California Workmen's Compensation law. During 1945 and 1946 the Executive Secretary of the Association served on a special study committee appointed by the Industrial Accident Commission to study the entire field of payment for medical services under the Workmen's Compensation law. In 1942 the Association itself filed and presented to the Industrial Accident Commission a petition for the establishment of a new minimum fee schedule. Several public hearings were held, at which the Association appeared on behalf of its members. In November, 1946, a new fee schedule was adopted. Since November, 1946, the Association has been active in conferences, and consultations with the Industrial Accident Commission, interested insurance companies, and others, in order to protect and maintain the minimum fee schedule for medical services rendered under the California Workmen's Compensation law.

Annual Session:

Once each year the Association holds an annual meeting to which the entire membership of the Association is invited. The meeting customarily lasts for four days. Scientific and technical exhibits are available for the members. The annual session is divided into two parts: the scientific assembly and the House of Delegates. The scientific assembly consists of all of the members of the Association and is divided into sections, each section representing a medical specialty. Each section holds meetings at which papers are presented and discussed relating to recent scientific advances in the particular specialty. General meetings of the entire scientific assembly are held, and customarily guest speakers of national prominence in medical fields are invited to present papers to the general assembly and the specialty sections. The House of Delegates, which meets during the annual session is, as previously stated, the legistive body of the Association. Regular annual meetings were held in 1945, 1946 and 1947. One of the issues of CALIFORNIA MEDICINE attached hereto contains the "Pre-Convention bulletin" for the 1947 annual meeting, and from it the nature and extent of the scientific program at the annual session may be ascertained.

Miscellaneous Activities:

In addition to carrying on routine duties and handling correspondence from members on a variety of subjects, the officers and employees of the Association represent the Association at meetings of various groups and agencies and maintain contacts with governmental agencies administering public health and other programs related to the practice of

medicine, in order that there may be maintained a proper coordination between such activities and the members of the medical profession. The miscellaneous activities of the Association, through its officers and employees, encompass such a tremendous volume of work that it is impractical to detail each activity. The following, however, are examples of these miscellaneous activities: Maintenance and furnishing of data on availability of hospital services and health insurance plans, medical schools, physicians who are certified specialists, institutions providing specialized care for the mentally ill, vital statistics, and many other like services.

II. DUES AND DUES-PAYING MEMBERS

The rate of dues in effect during each of the years 1945, 1946 and 1947 and 1948, and the number of dues-paying members each year are as follows:

Year	*Dues*	*Dues-paying Members*
1945	$ 20	6108
1946	$100	7528
1947	$100	8675
1948	$ 60	8699

During 1945 and to some extent in 1946, the number of dues-paying members was considerably less than the total active membership of the Association, because during the war years dues were waived entirely for all active members serving in the armed forces. As a consequence of the waiver of dues for military service which was effective during the years 1942 to 1946, inclusive, the revenues of the Association were considerably reduced under the normal prewar years.

North Bay Postgraduate Seminar

Benign Gastro-Intestinal Disease was the subject of a full day seminar held by the California Medical Association Postgraduate Committee at Santa Rosa, June 18, for the five north bay counties of Sonoma, Marin, Napa, Lake and Mendocino. A faculty of four teachers from San Francisco presented the material. Two cases presented at the morning Clinical Conference Session by the Staff of the Sonoma County Hospital provided a practical basis for discussion of ulcerative colitis and peptic ulcer.

PROGRAM

10:00 A.M.-12:00 Clinical Conference
1:30 X-Ray Diagnosis of Peptic Ulcer—Ivan J. Miller, M.D.
2:30 Peptic Ulcer, Clinical Diagnosis and Medical Management—Hugh Rose, M.D.
3:30 Peptic Ulcer, Recent Advances in Surgical Treatment—Roy Cohn, M.D.
4:30 Motion Picture: "Subtotal Gastrectomy for Perforating Duodenal Ulcer."
7:00 Dinner and Evening Session.
8:00 Non-Surgical Diseases of the Colon—Hugh Rose, M.D.
8:30 Surgery of the Colon—Victor Richards, M.D.

Doctor Ivan Miller, radiologist, emphasized the importance of careful evaluation of x-ray films in diagnosis of peptic ulcer, pointing out the factors leading to errors in diagnosis. He advocated examination of the patient without a preliminary barium meal, and urged that no gastric analysis or other irritating procedures be carried out immediately before x-ray examination. Gastric and duodenal herniae, hiatal hernia and colon lesions were discussed and illustrated by representative films. The speaker stressed the difficulties in the x-ray diagnosis of ulcerative colitis but pointed out the importance of the characteristic "granular mucosal pattern in a tubular appearing colon."

Dr. Hugh Rose, Jr., discussed the diagnosis and treatment of peptic ulcer. He emphasized the fallacy of relying too much upon the history, as in only 17 per cent of cases in which the diagnosis has been proven have the patients had a history classically indicative of the disease. Gastric analysis, x-ray and gastroscopy are important adjuncts in arriving at an accurate diagnosis, but each has its limitations, Dr. Rose said. It is therefore necessary to evaluate carefully the results of all available means of diagnosis and to supplement by repeated examinations. Treatment, the speaker said, is based upon proper balancing of the acid-base equilibrium, frequent feeding of easily assimilable foods, and inhibition of the pepsin activity through avoiding roughage, condiments and alcohol except in diluted forms. Dr. Rose also discussed the recent work done on an ulcer preventing factor, Vitamin "U," found in vegetable juices, particularly cabbage. The addition of adequate amounts of the raw juice to the diets was followed by a definite improvement in the rate of healing of experimentally produced ulcers in animals and of ulcers in a small series of patients.

Dr. Roy Cohn outlined the important factors in surgical procedures of the esophagus and stomach. He pointed out the recent reduction in surgical mortality in patients operated upon for ulceration of the lower one-third of the esophagus. As to gastric ulcer, he said that inasmuch as 14 per cent of demonstrable gastric ulcers are malignant, surgical resection should be considered for any lesion of the stomach that does not heal after four weeks of adequate medical treatment. He also reviewed the physiological aspects of vagotomy, pointed out the difficulties presented by the 20 per cent of patients having diffuse vagal trunks, and called attention to the poor results accruing from a combination vagotomy and resection. The two entities most amenable to vagotomy are marginal ulcer and gastro-jejuno-colic fistula, the speaker said. The indications for gastric resection, he said, are symptoms of obstruction and persistent or repeated hemorrhage. A careful evaluation of the patient must be made, with his age especially considered, as patients over 50 years of age are much more prone to exsanguinate. In the presence of massive gastric hemorrhage, a patient should receive 1000 cc. of whole blood immediately on diagnosis of the emergency. In case of persistent bleeding the patient should be explored immediately while receiving continuous blood transfusions for replacement of blood lost.

Dr. Cohn also discussed the treatment of hiatal hernia of the stomach. Calling attention to the relatively high incidence of recurrence following the usual types of operation, he briefly outlined the technique of herniotomy and repair by suture of the wall of the stomach to the diaphragm. This is a relatively simple procedure, he said, and as to the rate of recurrence, most satisfactory. Postoperative care, as outlined by the speaker, consists of maintaining gastric suction until restoration of peristalsis and relative healing of the anastomosis is established, ambulation on the first or second day postoperatively, fluid and electrolyte balance maintenance according to the patient's condition to insure a urinary output of 1000 cc. and 4 to 5 gm. of urinary chlorides which may be easily evaluated by use of a simple colorametric test for chloride. Penicillin is given, 40,000 units every three hours. Amino acids are not given parenterally, although oral administration is started early. Plasma is not considered physiological and, because of the danger of homologous serum jaundice, is not given.

In discussing the diagnosis of diseases of the colon Dr. Rose pointed out the common characteristic of vagueness of symptoms, the unreliability of results of single laboratory procedures, the advantage of air-contrast x-ray films of the colon, the necessity of proctoscopic and sigmoidoscopic examinations which provide a means for direct visual examination, for culture of ulcerative lesions and for biopsy. He stressed the importance of early surgical consultation in cases of ulcerative colitis resistant to medical treatment, in order to prevent the establishment of an irreversible chronic state. A hopeful recent development in the therapy of this disease, the speaker said, is the oral use of whole duodenal substance. Reports of this work have not been published, but communications regarding progress of reliable research are very encouraging, he said.

Dr. Victor Richards, discussing surgical operations on the colon, pointed out that, due to the sensory innervation, tenesmus is characteristic of lesions of the ano-rectal region, while obstruction is indicative of lesions in the sigmoid and transverse colon, and bleeding, anemia and loss of weight suggest the right colon as the site of malignant disease. The complications of obstruction, infection from perforation, fistulae, and hemorrhage were reviewed. The speaker outlined the surgical management of ulcerative colitis for the restoration of water, electrolyte and physiological equilibrium by ileostomy maintained for a period of one to four years or permanently, or resection of the colon in stages, with eventual ileorectal anastomosis. In the latter connection he reported on the experimental work done at Johns Hopkins of bringing the terminal ileum through the anal sphincter, and on Dennis' work in Minnesota using vagotomy in ulcerative colitis for relief of the spasms and resultant vicious cycle.

A total of 43 physicians attended the seminar from the five counties. The afternoon session was best attended, with 39 present. At the evening session the attendance was 26, and at the morning session, 18. The attendance from counties other than Sonoma was very light, with three each from Marin and Napa, and one each from Lake and Mendocino.

* * *

Announcement

Stanford University School of Medicine Postgraduate Courses for Practicing Physicians

September 6-10, 1948

Registration closes August 16, 1948. Fee $50.00 (Not covered by veterans' educational benefits.) Apply to Dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15, California.

Morning Courses, Monday through Friday, 8:30-12

Course 1. Surgical Emergencies and Fractures.
Course 2. Internal Medicine.
Course 3. Obstetrics and Gynecology.
Course 4. Psychosomatic Problems in Patients with Organic Disease.

Afternoon Courses, Monday through Friday, 1:30-5

Course 5. Cardiovascular Diseases.
Course 6. Proctology.
Course 7. Diseases of the Chest.
Course 8. Problems in Pediatrics.

General Meetings

Lane Hall—8 to 10 P.M.

Tuesday: Behavior Problems in Pediatrics, Dr. Hale F. Shirley.
Wednesday: Radioactive Isotopes in Medicine, Dr. R. R. Newell.

Council Meeting Minutes

Tentative Draft: Minutes of the 354th Meeting of the Council

Los Angeles, California, June 5-6, 1948.

The meeting was called to order by Chairman Bruck at 10 a.m., Saturday, June 5, 1948, in Conference Room No. 5 of the Biltmore Hotel, Los Angeles.

1. *Roll Call:*

Present were President Askey, President-Elect Kneeshaw, Vice-Speaker Charnock, Councilors Ball, Crane, Henderson, Anderson, Ray, Bruck, Lum, Pollock, Cherry, MacLean, Hoffman, Shipman, and Bailey, Secretary Garland and Editor Wilbur.

Absent: Speaker Alesen (illness); Councilors Green and Thompson (attending conflicting meetings).

Present by invitation were Dr. Dwight H. Murray, Chairman of the Committee on Public Policy and Legislation; Executive Secretary Hunton, Assistant Executive Secretary Wheeler; Legal Counsel Hassard; Public Relations Counsel Clem Whitaker; Mr. William M. Bowman, Executive Director of Cali-

fornia Physicians' Service; Mr. Ed Clancy of the Los Angeles office, Mr. Ben H. Read, Executive Secretary of the Public Health League of California, and county society executive secretaries Venables of Kern County, Donovan of Santa Clara County, Kihm of San Francisco County and Waterson of Alameda County.

Present by invitation during portions of the meeting were Dr. William L. Bender, Chairman of the Council's Committee on C.P.S. Fee Schedule, Dr. Paul Tully of the Association of Santa Fe Coast Lines Physicians' Association, and Drs. Forrest Gruningen and C. E. Atkins, representing the California Osteopathic Association.

2. *Minutes:*

(a) On motion duly made and seconded, the minutes of the 349th to 353rd meetings of the Council, held daily from April 10 to April 14, 1948, inclusive, were approved.

(b) On motions duly made and seconded, minutes of the 208th and 209th meetings of the Executive Committee, held April 14 and May 9, 1948, were approved.

3. *Appointment of Field Secretary:*

Following approval of the minutes of the May 9, 1948, meeting of the Executive Committee, in which approval had been given for locating the Association's Southern California office in Los Angeles, it was regularly moved, seconded and voted that Mr. Ed Clancy, Southern California representative, be given the title of Field Secretary.

4. *Membership:*

(a) A report of membership as of June 3, 1948, was received and ordered filed.

(b) On motion duly made and seconded, three 1947 delinquent members whose 1947 dues had been received since the last previous Council meeting, were ordered reinstated to active membership.

(c) On motion duly made and seconded, two hundred thirteen (213) members whose 1948 dues had been received since the last previous Council meeting were ordered reinstated to active membership.

(d) On motion duly made and seconded in each instance, three applicants for Associate Membership were granted Associate Membership. These were: Herman Nussbaum and Ruth A. Pillsbury of Alameda County, and Edmond V. Minasian of Yuba-Sutter-Colusa County.

(e) On motions duly made and seconded in each instance, the following sixteen (16) members were voted Retired Membership:

John Ohanneson, Alameda County.
H. A. Jacobson, Fresno County.
John H. Breyer, Los Angeles County.
G. Sherman Clark, Los Angeles County.
Glenn G. English, Los Angeles County.
William E. Hart, Los Angeles County.
Roscoe M. Nicholson, Los Angeles County.
Charles Edward Remaly, Los Angeles County.
Roy N. Taylor, Los Angeles County.
A. C. Willmott, Los Angeles County.
Henry W. Gibbons, Sacramento County.
Robert G. Pearson, Sacramento County.
Clarence E. Hyde, San Francisco County.
Hermon F. Wilson, San Francisco County
E. W. Mullen, Santa Clara County.
George H. Runckel, Siskiyou County.

(f) On motions duly made and seconded in each instance, Life Membership was voted for the following four applicants:

William J. Quinn, Humboldt County.
Martin G. Carter, Los Angeles County.
F. W. Rinkenberger, Los Angeles County.
Frank Krull, Sacramento County.

(g) The application of Dr. Deon A. Crew of San Luis Obispo for reconsideration of his earlier application for election to Life Membership was reviewed and it was agreed that such application would have to be made on the basis of existing provisions of the Constitution. It was regularly moved, seconded and voted that Dr. Crew be notified of the availability of Retired Membership in his case.

5. *Financial:*

(a) Reports showing bank balances as of June 3, 1948, balance sheet as of May 31, 1948, and receipts and expenditures for May and for the eleven months ended May 31, 1948, were received and approved.

(b) On motion duly made and seconded, it was voted that a Council committee investigate the possibility of the short-term investment of Association funds currently held. Doctors Kneeshaw and Ray were named by the Chairman as members of this committee.

6. *Referee for County Medical Society:*

A request was read from the Alameda County Medical Association that the Council appoint a referee to preside over the hearing of charges of unprofessional conduct brought against a member of that association. In accordance with the terms of Chapter 2, Section 3(a) (6) of the Association's By-Laws, the Council, on motion duly made and seconded, voted unanimously to appoint such a referee, the Executive Committee to select the referee as early as possible before the date of September 16, 1948, set for the hearing of the charges.

7. *A.M.A. "Grass Roots" Conference:*

After discussion of the conference of County Society Officers ("Grass Roots" Conference) of the A.M.A., it was regularly moved, seconded and voted that Dr. J. Frank Doughty of Tracy be asked to represent the Association at the conference of June 20, 1948.

8. *Public Relations:*

Mr. Whitaker reported on statements released to the press by State Insurance Commissioner Downey, in which critical comment was made on the activities of purveyors of voluntary forms of health insurance which tended to throw California Physician's Service into a false light. It was regularly moved, seconded

and voted that a letter sent by Mr. Hassard to Mr. Harold Haas, Deputy Attorney General representing the Insurance Commissioner, be approved and that Mr. Whitaker be authorized to take such steps as may be deemed necessary to counteract this type of statement.

9. *California Physicians' Service:*

Dr. Lewis T. Bullock appeared before the Council to suggest that certain changes be effected in C.P.S. fee schedules as they affect internists. He proposed that a committee of internists be appointed to meet with representatives of C.P.S. to this end. Dr. William L. Bender, Chairman of the Council's Committee on C.P.S. Fee Schedule, presented suggestions for changing certain sections of the existing fee schedule. Secretary Garland suggested that C.P.S. (1) establish a dual schedule of x-ray fees for specialists and general practitioners, (2) pay hospitals the same fees for x-rays as are paid to physician members of C.P.S. and (3) place an annual limit of a suggested $25 or $30 on the amount of x-ray services allowed beneficiary members.

Mr. Bowman presented the financial report of C.P.S. for April, 1948, pointing to an increasing balance in the unit stabilization (surplus) fund and an improved operating experience under present dues schedules and operating procedures.

Dr. Bender presented a tabulation of suggested fee schedule changes. On motion duly made and seconded, it was voted not to approve these suggested changes. It was regularly moved, seconded and voted that the Council give its C.P.S. Fee Schedule Committee full authority to proceed with a *complete revision of the present fee schedule*, the Council to recommend to the C.P.S. Board of Trustees that full consideration be given such suggestions.

It was regularly moved, seconded and voted that the Council request the C.P.S. Board of Trustees to establish a board of review to consider cases of apparent inequities among individual physician members of C.P.S.

10. *Association of Santa Fe Coast Lines Physicians:*

Mr. Hassard reviewed the status of the application of the Association of Santa Fe Coast Lines Physicians for adjudication of their demands on the Board of Directors of the Santa Fe Hospital Association for adjustment of compensation and other matters. He reported that the American Medical Association had not provided a representative for the Santa Fe physicians at the hearing of this matter before the National Railway Labor Board. Dr. Paul Tully, who appeared at this hearing, reported on the nature of the proceedings.

It was regularly moved, seconded and voted that Dr. Tully be reimbursed in the amount of $300 for the expenses of his trip to Chicago to make this appearance. It was regularly moved, seconded and voted that Dr. Dwight H. Murray bring before the Board of Trustees of the American Medical Association the displeasure of the Association at the A.M.A.'s failure to provide representation for Dr. Tully.

11. *Committee on Industrial Practice:*

Dr. Donald Cass, Chairman of the Committee on Industrial Practice, reported to the Council that the Industrial Accident Commission of the State of California had scheduled hearings for June 7 in Los Angeles and June 10 in San Francisco on an application of the Western Orthopedic Association for a review of certain of the items in the present schedule of industrial medical fees. Dr. Cass stated that his committee had nearly completed its work on a proposed revision of the fee schedule and suggested that the Association appear at these hearings and make such a report to the Commission. On motion duly made and seconded, it was voted to aprove this type of presentation to the Industrial Accident Commission, the Association to be represented by Dr. Cass, Messrs. Hassard and Hunton, and Hon. Sam L. Collins, associate legal counsel.

Dr. Cass also reported that he had been in touch with Dr. Christopher Leggo, Chairman of the special Committee on Industrial Health, and that the two committees planned to meet in order to delineate the areas of responsibility of the two.

12. *Recess:*

At this point, 5:45 p.m., the Council recessed until 9 a.m., Sunday, June 6, 1948.

13. *Reconvention:*

The Council reconvened in the same room at 9 a.m., Sunday, June 6, 1948.

14. *Roll Call:*

On roll call, all those noted present June 5 were present, with the exception of Councilor Bailey, absent at a Board of Medical Examiners meeting. Also present was Councilor Thompson. Present by invitation was Dr. Wilton L. Halverson, State Director of Public Health.

15. *California Medicine:*

Editor Dwight L. Wilbur of CALIFORNIA MEDICINE reported that Dr. Hamilton Anderson had tendered his resignation from the advertising committee of the publication and that Dr. Nelson Howard had been compelled to resign from the committee for health reasons. He suggested that the interim appointment of Dr. John W. Cline to succeed Dr. Howard be confirmed and that the committee avail itself of the services of Dr. R. W. Weilerstein of the Federal Food & Drug Administration and call upon Doctors Hamilton Anderson, Paul Hanzlik and C. H. Thienes as consultants in pharmacology. On motion duly made and seconded, these suggestions were voted approval.

Dr. Wilbur also outlined a proposal received from staff members of the University of Chicago to publish an annual review of medical progress, to be offered to readers of CALIFORNIA MEDICINE as a supplement or as a separate publication at a cost subscription rate. After discussion, it was regularly moved, seconded and voted that this review be made available to readers of CALIFORNIA MEDICINE on a voluntary basis if that is practicable.

16. *California Society of Allergy:*

Attention was called to the formation of the California Society of Allergy, which carries on its letterhead the phrase "A Section of the California Medical Association." It was pointed out that the 1948 House of Delegates had established a section on allergy but that this section was not empowered to adopt a separate society name. On motion duly made and seconded, it was voted that the Secretary notify the allergy society on this point and also advise the Bulletin of the Los Angeles County Medical Association, which had printed a letter from this society, that there was an ambiguity of titles involved in this situation.

17. *Palo Alto Clinic:*

A letter from a Palo Alto physician, calling attention to alleged defects in the contract for health care recently adopted by the Palo Alto Clinic and the Menlo School and Junior College, was read and it was agreed that no Council action was required since the contract had already been approved by the two county medical societies involved.

Further discussion was had on the advisability of notifying students of the availability of voluntary forms of medical care insurance and it was agreed the Secretary should take up with the Committee on Health and Public Instruction the matter of presenting to college students suitable material along these lines.

18. *Blood Banks:*

The Chairman read a report from Dr. John R. Upton, chairman of the blood bank commission, outlining the activities of the commission in the past two months. No action required.

19. *1948 House of Delegates:*

Discussion was held on various decisions of the 1948 House of Delegates which required Council action to put into effect.

(a) In regard to the amendment to Section 1, Article XI, of the Constitution, providing for reduction or waiver of dues in special cases, it was regularly moved, seconded and voted that subsection (b) of this section be governed by the words "War Service" in the title in order to provide a waiver of dues for members in military service.

(b) In regard to the reduction of dues in special cases (subsection (c)) it was regularly moved, seconded and voted that a committee of three Council members prepare schedules of recommended dues and report back to the Council. The chairman named Dr. Kneeshaw as chairman of this committee, Doctors Charnock and Anderson as members.

(c) In regard to subsection (g) of Section 1, Article XI, it was regularly moved, seconded and voted that minimum dues of $3 per year be applied to all eligible membership classes mentioned in the section and that the Secretary notify the county medical societies that such classes of membership are now available.

(d) In regard to Resolution No. 8, relative to additional training and teaching facilities, it was regularly moved, seconded and voted that the deans of the five medical schools of California, or their representatives, be appointed a committee to study this problem.

(e) In regard to Resolution No. 10, relative to corporate practice of medicine, it was regularly moved, seconded and voted that the Council appoint a committee to study this matter and report back to the Council prior to its first meeting in 1949. The chairman, with the consent of the Council, named Dr. Wilbur Bailey as chairman of this committee, with Doctors Dell Lundquist, Russel V. Lee, Lewis T. Bullock, and Robert Blackmun as members.

(f) In regard to Resolution No. 11, relative to compensation of physicians in tax-exempt hospitals, it was regularly moved, seconded and voted that the resolution be referred to the Committee on Public Policy and Legislation, with the request that this committee seek the assistance of the Association of California Hospitals in taking the required legislative steps to correct present inequities.

(g) In regard to Resolution No. 14, relative to wider choice of physicians by injured workmen, it was regularly moved, seconded and voted that the matter be referred to the Committee on Industrial Practice, with the request that the committee confer with Dr. F. J. Gaspard of Los Angeles, maker of the original resolution.

(h) In regard to Resolution No. 21, relative to the system of coroners' examinations, it was regularly moved, seconded and voted that this subject be referred to the Committee on Public Policy and Legislation.

(i) In regard to Resolution No. 23, relative to operation of the Crippled Children's Act, it was regularly moved, seconded and voted that the Executive Committee confer with the State Director of Public Health in order to clarify the situation.

(j) In regard to Resolution No. 24, relative to mental hygiene clinics, it was regularly moved, seconded and voted that the legislation authorizing the establishment of mental hygiene clinics be investigated.

(k) In regard to Resolution No. 26, relative to payment by California Physicians' Service for radiological services in hospitals, it was regularly moved, seconded and voted that copies of this resolution be sent to all hospitals in California.

20. *Hospital Construction:*

The Council discussed a proposed statement which outlined the various types of hospitals which might be built in California, the sources of funds available for each type and the advantages and disadvantages of the several types of financing. It was regularly moved, seconded and voted that this statement be adopted as presented and that copies of it be sent to all component county societies, together with an explanatory letter.

21. *State Department of Public Health:*

Dr. Wilton L. Halverson, State Director of Public Health, discussed the publication by his department of a list of 198 proposed "health centers" and pointed out that this list represented an ideal distribution of

centers for the use of local health authorities and was not actually a plan of his department. He also discussed the allocation of hospital construction funds, state and federal, which is under the jurisdiction of his department, and stated that the representatives of the State Department of Public Health were not campaigning for or against any specific type of hospital.

22. *California Society for Crippled Children:*

Mrs. Fred Markham and Mrs. E. E. Smith appeared before the Council and presented the proposed program of the California Society for Crippled Children for establishment of a program to detect and control epilepsy. They stressed the fact they wished to work with the physicians and the county or local medical societies. After discussion, it was regularly moved, seconded and voted that the Council Chairman prepare a set of standards to apply to this program and report back to the Council.

23. *Fee for Legal Services:*

Mr. Hassard presented a statement for extraordinary legal services, as approved by the Council and House of Delegates in establishing the budget, in the amount of $2,000. On motion duly made and seconded, this statement was approved for payment.

24. *California Joint Committee on School Health:*

An invitation for the Association to be represented at the June 21-July 9 session of the California Joint Committee on School Health, sponsored by the State Department of Education, was approved and the chairman authorized to name a representative for this conference.

25. *Emblems for Members of 50-Year Standing:*

The Executive Secretary reported that the Association's records of membership do not extend back fifty years and, accordingly, no members' names were available for distribution of 50-year membership emblems as approved by the House of Delegates. It was agreed that the records of the county medical societies would be accepted for this purpose.

26. *National Health Assembly:*

A resolution adopted by the Council of the Utah State Medical Association, criticising the appropriation of funds by the American National Red Cross and other organizations which rely on publicly-contributed funds, for purposes of promoting the National Health Assembly, was approved in principle and the California Delegates to the A.M.A. authorized to support such a resolution in the A.M.A. House of Delegates.

27. *Ethics in Eyeglass Dispensing:*

A letter was read from a member in Fresno, outlining several methods proposed for the dispensing of eyeglasses in an ethical manner. It was agreed that the best solution presented was the encouragement of additional optical companies to locate in the area.

28. *Pathological Laboratory:*

A letter was read from a member seeking an opinion on the incorporation of a pathological laboratory to serve the physicians of his community. It was regularly moved, seconded and voted that the member be advised that the incorporation of such a laboratory presented ethical considerations which might best be met by the physician operating his own laboratory without forming a corporate structure.

29. *Time and Place of Next Meeting:*

It was agreed that the next meeting of the Council should be held in San Francisco on August 21 and 22, 1948.

Adjournment.

L. Henry Garland, M.D., *Secretary*

Edwin L. Bruck, M.D., *Chairman*

In Memoriam

Davis, Joseph Paul, Jr. Died in Turlock, May 20, 1948, age 33, of a heart attack. Graduate of the University of Oklahoma School of Medicine, Oklahoma City, 1942. Licensed in California in 1943. Doctor Davis was a member of the Stanislaus County Medical Society, and the California Medical Association.

✤

Ogden, James Cheston. Died in Long Beach, May 25, 1948, age 45, of injuries suffered in a fall from the roof of his apartment house. Graduate of the State University of Iowa College of Medicine, Iowa City, 1930. Licensed in California in 1937. Doctor Ogden was a member of the Los Angeles County Medical Association, the California Medical Association, and Fellow of the American Medical Association.

✤

Reiss, Oscar. Died in Beverly Hills, June 17, 1948, age 65, of coronary thrombosis. Graduate of the University of Illinois College of Medicine, Chicago, 1906. Licensed in California in 1913. Doctor Reiss was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

Schurmeier, Harry Leach. Died in Santa Barbara, May 12, 1948, age 65, of a myocardial infarction. Graduate of Northwestern University Medical School, Chicago, Illinois, 1911. Licensed in California in 1913. Doctor Schurmeier was a member of the Santa Barbara County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

Snure, Henry. Died in Los Angeles, May 17, 1948, age 71. Graduate of the University of Louisville School of Medicine, Kentucky, 1910. Licensed in California in 1916. Dr. Snure was a retired member of the Los Angeles County Medical Association and the California Medical Association.

✤

Walker, Calvin Albert. Died in San Francisco, May 18, 1948, age 73, of a heart attack. Graduate of the Cooper Medical College, San Francisco, 1905. Licensed in California in 1905. Dr. Walker was a member of the San Francisco County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

Walsh, Joseph Francis. Died in Eureka, May 28, 1948, age 63, of a heart ailment. Graduate of the Cooper Medical College, San Francisco, 1909. Licensed in California in 1909. Doctor Walsh was a member of the Humboldt County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Announcement of the award of a $300 nurses' training scholarship to Shirley Van Ness, a student at Castlemont High School, was made recently by the Woman's Auxiliary to the Alameda County Medical Association. The scholarship was offered by the auxiliary as a part of its intensive program to stimulate interest in nursing as a profession. In an effort to help overcome the shortage of nurses, the auxiliary has also sponsored a poster contest in Alameda County schools to emphasize the attractiveness of nursing, and has arranged for speakers to address girls of high school age on the subject.

CONTRA COSTA

In the June issue of California Medicine it was erroneously reported that Dr. Edwin W. Merrithew was to retire as county health director on July 1. Actually his retirement was from the position of county physician and medical director of the county hospital. He did not serve as county health director.

DEL NORTE

The Humboldt County Health Department has extended its service to Del Norte County under an agreement with the board of supervisors of the latter. The agreement provides that the Humboldt department will extend its facilities to Del Norte County, which will pay a percentage of the expenses based on county population. Dr. Kenneth W. Haworth, with headquarters in Eureka, will serve as physician for both counties.

LOS ANGELES

Sharing in new grants-in-aid totalling $16,000 awarded by the National Vitamin Foundation to support researches, is the University of Southern California Medical School. The grant is to assist Dr. E. Geiger, professor of pharmacology and toxicology, in investigations to determine the effects of time elements on the utilization of water soluble vitamins.

* * *

The mid-winter conference on Microscopic Tumor Pathology will be held Sunday, November 21, at the Los Angeles County General Hospital. Dr. A. Purdy Stout, Columbia University College of Physicians and Surgeons, will be chairman of the conference, and Dr. Louisa Keasbey, secretary. Dr. Keasbey will contact pathologists in California for cases for the conference. Reservations should be made with her at 1200 North State Street, Los Angeles 33.

Dr. Stout will also appear on the program of the refresher course at the Los Angeles County General Hospital on November 22-23. Dr. Justin Stein, 1407 South Hope Street in Los Angeles, is chairman of the committee that will have charge of the arrangements for the refresher course.

MERCED

The City of Los Banos in Merced County recently made arrangements to have its public health service requirements taken over by the County Health department. Formerly the town had its own health service under the supervision of Dr. L. R. Hillyer.

SAN BERNARDINO

The City of San Bernardino has set up a full-time health department with Dr. Warren Fox, formerly health officer of Riverside County, as director. Until the department began operating on a full-time basis, Dr. Finnis E. Wiggins was part-time health officer for the city. Dr. Robert S. Westphal, former deputy city health officer of Rochester, N. Y., has been appointed to the county post vacated by Dr. Fox.

SAN FRANCISCO

A gift of $41,000 for a fellowship in opthalmology has been received by Stanford University from Upsilon chapter of the Delta Gamma sorority. Mrs. David Packard, president of the Stanford Delta Gamma Association, said that the money represented proceeds of the sale of the sorority house following dissolution of Stanford sororities in 1944.

* * *

Dr. Emile Holman, professor of surgery at Stanford University Medical School, was elected second vice-president of the American Surgical Association at a recent meeting.

* * *

With the opening of a ward for patients offering themselves for research in cancer in the Laguna Honda Home operated by the San Francisco Health Department, the University of California Laboratory for Experimental Oncology has gone into full operation.

A four point program of the laboratory includes the study of electronic characteristics of normal and malignant growth; investigation of the nature of changes in the whole body brought about by cancer; the experimental chemical treatment of cancer with new agents; and a fundamental study of the characteristics of human malignant tissue. Work at the laboratory is under the direction of Dr. Michael Shimkin, professor of experimental oncology, and he is assisted by Dr. Howard R. Bierman, associate professor of experimental oncology.

The laboratory is a cooperative venture of the University's Medical School and the National Cancer Institute, financed by the U. S. Public Health Service. It was established in January, 1947.

STANISLAUS

A report on findings in gynecological researches was given by Dr. Daniel G. Morton, associate professor of gynecology at the University of California Medical School, at a recent meeting of the Stanislaus County Medical Society in Modesto. In a business session at the same meeting, Dr. Richard Husband was appointed as the society's advisor to the Omega Nu sorority to assist the sorority in the distribution of funds its has collected to aid handicapped persons in the community.

TEHAMA

Dr. James Faulkner recently replaced Dr. O. T. Wood as health officer for the City of Red Bluff.

GENERAL

Among appropriations for the University of California building program by the 1948 legislature were $500,000 for

a virus laboratory at Berkeley and a $5,000,000 for Medical School expansion at Los Angeles.

* * *

The 16th annual meeting of the Central Association of Obstetricians and Gynecologists will be held in Denver, September 23, 24 and 25, 1948.

* * *

The first annual meeting of the American Association of Blood Banks will be held August 26, 27, and 28, at the Hotel Statler, Buffalo, N. Y. Further information may be obtained from the office of the secretary, 3301 Junius Street, Dallas 1, Texas.

* * *

The Surgeon General of the Navy has announced the expansion of the professional training program for reserve and regular medical officers to permit more Navy doctors to meet the requirements of certification by the various American Specialty Boards, and to encourage the young doctor to intern under the auspices of the Navy. Graduates of Class A medical schools who have been accepted for internship by a hospital approved for such training by the Council on Medical Education and Hospitals of the A.M.A. may be commissioned as Lieutenants (junior grade) and permitted to continue their intern training. After completing their internships, the medical officers must remain on active duty for a period of one year. If they meet the professional, physical and moral requirements, they will be encouraged to transfer to the regular Navy.

Resident physicians now in civilian hospitals, or those accepted for approved residency training, are eligible for commissions in the regular Navy. Those so commissioned will be assigned to duty, with full pay and allowances, in the hospital in which they are already a resident or to which they have been accepted for residency training.

Information concerning any part of the program may be obtained by writing to the Chief of the Bureau of Medicine and Surgery, Navy Department, Washington 25, D. C.

The American Congress of Physical Medicine will hold its 26th annual scientific and clinical session September 7, 8, 9, 10 and 11 inclusive, at the Hotel Statler, Washington, D. C. All sessions will be open to members of the medical profession in good standing with the American Medical Association. In addition to the scientific sessions, the annual instruction courses will be held September 7, 8, 9 and 10. Full information may be obtained by writing to the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

* * *

The American College of Physicians announces that a limited number of fellowships in medicine will be available from July 1, 1949 to June 30, 1950. These fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in internal medicine. The stipend will be from $2,200 to $3,200.

Application forms are obtainable from The American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa., and must be submitted in duplicate not later than November 1, 1948. Announcement of the awards will be made as promptly as is possible.

* * *

Grants of more than $121,000 in Federal funds for research in cancer, allotted among the University of California, Stanford University and the College of Medical Evangelists in Los Angeles, were approved last month by the Advisory Cancer Council and the U. S. Public Health Service. The University of California Medical School in San Francisco received $85,064, Stanford University $11,134, the College of Medical Evangelists $17,419, the University of California in San Francisco $5,535 and the University of California at Berkeley $3,419.



INFORMATION

Practice of Medicine by Private Nonprofit Hospitals Held Illegal

Recently, the State Board of Medical Examiners requested the opinion of Fred N. Howser, Attorney General of California, as to whether a private nonprofit hospital is permitted by law to practice medicine, and, if not, as to whether such a hospital could legally employ a pathologist on a salary basis.

On May 19, 1948, the Attorney General rendered an opinion to the State Board of Medical Examiners, holding, first, that a private nonprofit hospital may not practice medicine, and, second, that the employment on a salary basis of a pathologist by such a hospital would constitute the unlawful practice of medicine by the hospital.

The opinion, in full, follows:

OPINION of
Fred N. Howser, Attorney General
E. G. Funke, Deputy Attorney General

The Board of Medical Examiners has submitted the following questions:

1. Is a corporation or an association of laymen operating a private, nonprofit hospital permitted to practice any system or mode of treating the sick or afflicted in this State?

2. If a corporation operating a private, nonprofit hospital enters into a contract with a physician under which the physician will perform professional services in the hospital and receive a fixed salary, and the corporation will thereupon bill the patient for the professional services rendered by the physician at rates that have no bearing on the physician's salary, is the corporation violating any of the provisions of the Medical Practice Act?

The conclusions reached are summarized as follows:

1. No one is permitted to practice any system or mode of treating the sick or afflicted in this State unless he is licensed in accordance with the provisions of section 2000 et seq., Business and Professions Code. Corporations or other artificial legal entities are specifically mentioned in section 2008 as having no professional rights, privileges or powers, and may therefore not be licensed to so practice.

2. The employment of a licensed physician by a corporation and the subsequent billing of the patients by the corporation, as referred to in the second question, would constitute illegal practice of a system or mode of treating the sick or afflicted in this State and is therefore prohibited by law.

ANALYSIS

The Board of Medical Examiners advises that a private, nonprofit hospital operating in the State and owned by a corporation, contemplates entering into a contract with a duly licensed physician and surgeon who specializes as a pathologist. They propose that the physician and surgeon will perform professional services for hospital patients and receive therefor a fixed salary. The corporate owner of the hospital proposes to separately bill each private patient for the professional services that have been rendered to such private patient by the pathologist. They propose that such charges are to be independent of the ordinary regular charge for hospital bed, board and usual hospital services and further, that the rate of charge will have no bearing on the salary that the pathologist will receive from the corporation.

The courts have made it abundantly clear, as is hereafter shown, that corporations are prohibited from engaging in the practice of any system or mode of treating the sick or afflicted in this State. The pronouncements of the courts also, in our opinion, require the conclusion that the arrangement contemplated by the hospital in question falls within the same prohibition.

The California Legislature has enacted a Corporations Code. In the Corporations Code there are found various provisions governing the formation, powers and duties of corporations as a whole. Since a corporation is a "creature created by statute," it has only such powers as the statutes give to it. Nowhere in the Corporations Code is a corporation given specific authority to practice the healing arts.

We must, of course, call attention to the fact that certain nonprofit corporations may be formed for the purpose of defraying or assuming the cost of professional services of licentiates of the healing arts. Section 9201, Corporations Code, formerly Section 593(a) Civil Code, so provides. However, the same section except as expressly permitted therein does not authorize the formation of any corporation for the purpose of rendering the professional services regulated by Division 2 of the Business and Professions Code. Likewise, Chapter 1 of Division 2 of the Health and Safety Code, governing the operation of clinics and hospitals, specifically provides (section 1214) that the provisions of said chapter do not authorize any person other than a licentiate of a healing art to engage *directly or indirectly* in the practice of medicine.

The opinion of the Supreme Court in California Physicians' Service v. Garrison, 28 Cal(2d) 790, construed the provisions of Corporations Code 9201, formerly Civil Code 593(a), and particularly the authorizing of the incorporation of a physicians' service. The court therein states (page 802): "the Legislature, by enacting section 593(a) of the Civil Code, expressly authorized the organization of cor-

porations such as California Physicians' Service. By this enactment *the state's social policy in regard to the corporate practice of medicine, to the limited extent specified, has been determined* and the courts are bound thereby. [Emphasis added.]

Further, a corporation, although considered by law as a legal entity, and to have in many respects all the rights and privileges of an individual person, nevertheless is physically unable to fulfill the educational requirements or to take the examination required of all persons who seek to secure a license to practice the healing arts. Thus, even though section 2008, Business and Professions Code, did not specifically state that a corporation has no professional standing, nevertheless it would be a physical impossibility for a corporation to be a licentiate of a healing art.

Our courts have on numerous occasions held that a corporation may not engage in the practice of medicine. The opinion of the Supreme Court in Pacific Employers Insurance Co. v. Carpenter, 10 Cal. App. (2d), 592, 594, contains a comprehensive discussion which is pertinent. The following quotation summarizes the court's views on this subject:

"It is well settled that neither a *corporation nor any other unlicensed person or entity may engage, directly or indirectly*, in the practice of certain learned professions including the legal, medical and dental professions. [Cases cited.] Under the foregoing authorities it is clearly declared unlawful for a corporation to indirectly practice any of said professions for profit by engaging professional men to perform professional services for those with whom the corporation contracts to furnish such services. In other words, said authorities declare that said professions are not open to commercial exploitation as it is said to be against public policy to permit a 'middleman' to intervene for profit in establishing the professional relationships between the members of said professions and the members of the public." [Emphasis added.]

In People v. Pacific Health Corporation, 12 Cal (2d), 156, 158, the court stated that: "It is an established doctrine that a corporation may not engage in the practice of such professions as law, medicine or dentistry." [citing cases.] The appellant, Pacific Health Corporation, contended, however, that it did not itself undertake to perform medical services, but merely to furnish competent physicians; that the physicians and surgeons were not to be employed by it on a salary basis, nor directed by it, but were to be compensated for actual professional services after they were rendered; and the corporation's theory was that the doctors, under its arrangement, were to be independent contractors and that, therefore, the corporation would be absolved of the charge of practicing medicine. The court said:

"We are unable to agree that the policy of the law may be circumvented by technical distinctions in the manner in which the doctors are engaged, designated or compensated by the corporation. The evils of divided loyalty and impaired confidence would seem to be equally present whether the doctor received benefits from the corporation in the form of salary or fees. Any freedom of choice is destroyed, and the elements of solicitation of medical business and lay control of the profession are present whenever the corporation seeks such business from the general public and turns it over to a special group of doctors."

This argument that the mere ownership of a hospital where medical services are rendered by the owners' licensed employees does not in itself constitute the practice of medicine (i.e., that the practice of medicine involves actual treatment of persons), was also rejected by our courts when applied to the practice of dentistry. See Painless Parker v. Board of Dental Examiners, 216 Cal. 285, 296. Appellant in that case contended that there was a distinction between the practice of dentistry which the statutes undertook to regulate, and the purely business side of the practice and that the management and conduct of the business side by a layman was not prohibited by the statute, and that such attempted prohibition would be unconstitutional. We refer to the well considered opinion of the court, wherein are given the reasons for the rejection of this contention made by appellant.

It may be contended that the pathologist in the situation presented would merely examine and diagnose an illness and therefore would not be practicing medicine. But our courts have held that diagnosis is as much a part of the practice of medicine as is the administration of remedies. In fact, section 2141, Business and Professions Code, declares that one who diagnoses any illness is engaging in the practice of medicine (see People v. Jordan, 172 Cal. 391).

Throughout the opinions cited one will note that the courts have indicated that the practice of medicine by corporations for profit, through the employment of licensed physicians, has a tendency to debase the profession, is not in the interests of the safety, health and welfare of the public, and therefore is contrary to public policy. The right to practice medicine and surgery under a license by the State is a personal privilege. It cannot be delegated. Therefore, a corporation or other unlicensed person may not engage in the practice of medicine by employing one who is licensed to do the things which constitute the practice of the profession. Were the rule otherwise, one would find a licensed physician accepting directions and instructions in the diagnosing and treating of ailments from a corporation or from an individual who is not a licensed practitioner.

BOOK REVIEWS

LABORATORY TECHNIQUE IN BIOLOGY AND MEDICINE. By E. V. Cowdry, Professor of Anatomy, Washington University, and Director of Research, The Barnard Free Skin and Cancer Hospital, St. Louis, Missouri. Pp. 269. Williams and Wilkins Company, Mt. Royal and Guilford Avenues, Baltimore 2, Maryland, 1948. Price, $4.00.

Under the present title, this book is the second revised edition of the author's former book entitled *Microscopic Technique*. It is an alphabetically arranged compilation of qualitative and quantitative micro-tests and techniques applicable to tissues, organs, body fluids, unicellular organisms, bacteria, etc., useful in routine diagnosis, physiological research, microscopic study, toxicological examinations and other laboratory work. No detail has been overlooked. The techniques described are of proved value and most of these were revised by their originators. Sufficient detail is given to enable an experienced person to proceed without difficulty. Many references to original papers for further details are included. When micro-technique is not applicable, other procedures are suggested, for instance, use of a spectrophotometer or spectrograph, etc. Outstanding is a lengthy and detailed description of Knisely's quartz rod technique for examining living organs *in vitro*, especially the capillary circulation, a valuable method in a wide variety of physiological problems. All in all this edition is remarkably complete in content and scope. It is a must for hospital technicians, researchers in biological and medical sciences and clinical pathologists.

ENCYCLOPEDIA OF MEDICAL SOURCES. By Emerson Crosby Kelly, M.D., F.A.C.S., Associate Professor of Surgery, Albany Medical College, attending surgeon, Albany Hospital Editor, Medical Classics. The Williams & Wilkins Company, 1948. Price, $7.50.

The author has made available an informative volume not only for those who are interested in medical history, but also for those who desire precision in regard to medical eponyms. At the same time he has compiled a magnificent bibliography of the important contributions to medicine and surgery for those who wish to write papers for the clinician. The volume constitutes an indispensable repository of fundamental bibliographic information and makes possible for writers the saving of untold hours of library research. The author puts upon a sound historical and bibliographic basis the true but often falsely quoted works of the great clinicians, whose original and pertinent references are made easily available. For those who find the dictionary enjoyable reading, "The Encyclopedia of Medical Sources" will offer similar entertainment although it was originally intended as a source book.

PROCEDURE IN EXAMINATION OF THE LUNGS. Kraetzer, Third Edition, Oxford Medical Publications. 1947. $3.50.

This book has long been a most valuable aid to the student in becoming oriented on the chest, something which many graduates have never learned. It has also served to emphasize a phase of examination which there has been a tendency to ignore since the more recent refinements of roentgenography and the emphasis on its peculiar value in the diagnosis of early tuberculosis. We have heard not a few papers and discussions minimizing or ignoring the physical examination of the chest in this connection, overlooking the fact that there are a number of conditions in which the x-ray gives us no information. In his enthusiasm for mass surveys the tuberculosis clinician is at times prone to lose sight of the fact that the purpose of the examination is to detect any pathological condition in the patient's chest, not simply whether he has tuberculosis or not. Bronchitis, bronchiolitis, asthma and beginning bronchostenosis from tuberculosis or other cause are only a few of the conditions whose recognition is not helped by the x-ray.

It is, however, disappointing to find some of the omissions of the former editions carried forward into this one. Failure to mention the heart in the chapters dealing with inspection and palpation is one of the minor but obvious deficiencies. The continuation of some outmoded findings such as Kroenig's isthmus is also unfortunate.

The discussion of the causes of spontaneous pneumothorax is in need of revision.

Dr. Segal contributes a very valuable appendix in an attempt to bring the book up to date.

It is obvious that the addition of an appendix, however good in itself, is not sufficient justification for calling this a new edition. It is to be regretted that a firm with the standing of the Oxford Medical Publications should be guilty of such a breach of faith with its clientele, a practice which is bound to react unfavorably on its reputation in regard to future publications.

THE LUNGS. William Snow Miller, M.D., F.C.D. Sc. Second Edition. Charles C. Thomas, Springfield, Ill. $7.50.

Ever since the first edition of this book appeared in 1937 it has been the vade mecum for those who would understand the physiology and pathology of the lungs. Those whose small individual financial contributions made possible the summarizing of the lifetime work of the author are entitled to feel a degree of pride in the presentation which has been achieved.

Within the limits of a book of this size it has not been possible to incorporate all his work. This edition, which contains an added number of color plates, black and white illustrations and manuscripts, is to that extent an improvement on its predecessor. It is hoped that still more may be included in a future revision.

The outstanding quality of the color plates of the first edition has been well maintained in the second.

PRACTICAL METHODS IN BIOCHEMISTRY. Fifth Edition. F. C. Koch and Martin E. Hanke, University of Chicago, pp. 419, ix prelims. Williams and Wilkins Co., Baltimore, 1948. Price, $3.00.

This book is a happy compromise between one widely used laboratory guide of 1,321 closely printed pages and another of 149 pages. Since the three books endeavor to serve the same end and, indeed, carry virtually the same title, somewhat of a comparison may be worth while. Both the "Fat" and the "Thin" contain sections on Milk and Ephithelial and Connective Tissues. Koch and Hanke chose to omit these, and wisely so, in the judgment of the reviewer; the experiments usually performed on these materials are dull, uninformative, and seldom illustrate any point of fundamental importance. "Fat" contains a good section on enzymes which, because of its emphasis on general enzyme biochemistry, is a good prelude to the chapters on digestion and might well be included in other good laboratory manuals in biochemistry. Koch and Hanke included, of course, the usual chapters on digestion and did so quite concisely in about half the space. The authors devoted 145 pages to blood and urine

in contrast to the 73 pages in "Thin" and the 392 pages in "Fat." Koch and Hanke's book is a straightforward, practical laboratory manual, while "Fat" is, admittedly, a substantial reference book as well. In the reviewer's opinion, Koch and Hanke have turned out a thoroughly good manual in which the subject matter is well balanced as to division of space. The book has run through four previous editions and, hence, is almost free of typographical errors (*steriod* on page 347 and *untable* on page 65). It contains two excellent chapters, totalling 50 pages of experiments, on Vitamins and Microbiological Assays. These are very timely subjects and, as far as the reviewer knows, are not to be found in any other laboratory book intended for the introductory student of biochemistry.

The appendix describes in greater detail than does its fat companion the preparation of the numerous reagents required for laboratory instruction in biochemistry. It is unfortunate that it does not contain, as does the larger work, a section on the maintenance of laboratory animals for experiments in nutrition. Such material reminds the student of our indebtedness to the rat, the guinea pig, etc. and indicates to those who enter upon the study of medicine the fundamental importance of animal experimentation in medical research.

The book is not without its other faults but to the reviewer, they are comparatively few and, in some cases, trivial. As in almost all laboratory manuals an experiment is to be found on the Lobry de Bruyn and van Ekenstein rearrangement. Fortunately, the authors do not suggest that this is of any biological significance; to minimize the possibility of concluding, by implication, that fructose and mannose are by this means converted to glucose, in vivo, it would be well in future editions to mention the role of phosphorylation in effecting the fructose-to-glucose conversion.

In the determination of nitrogen in blood and urine, emphasis is given to direct Nesslerization methods. With sufficient practice, and when employed by experienced technicians, these methods may be used with confidence. The reviewer, however, has seldom found that they were satisfactory for the usual large class of medical students: a gross precipitate or a troublesome opacity frequently develop on Nesslerization. Since rapid, accurate, semi-micro, Kjeldahl and steam-distillation methods are readily available, these are to be preferred, in the reviewer's opinion, for the determination of urea, total nitrogen, and non-protein nitrogen.

In many instances the authors offer a choice of methods. They do so usually without appraisal and without giving to the reader the benefit of their years of experience in biochemistry. This fault is not peculiar to the book by Koch and Hanke, for seldom indeed does it happen that analytical methods are presented in laboratory manuals on biochemistry according to any rating system.

The text contains a few curious constructions which may disturb a grammarian insistent upon purity of syntax. For example, on page 39, should not the phrase "dissolve this in a test tube in about 6 cc. 95 per cent alcohol" be changed to read "dissolve this in about 6 cc. of 95 per cent alcohol contained in a test tube"? On page 115 we read "the pH's appear too acid." Surely this should be "the pH's appear too low" or "the solutions appear too acid."

"Saccharose" is used throughout the text in place of "sucrose" except on page 143, where, for no apparent reason, the much more popular "sucrose" comes into its own.

There are many needless inconsistencies in the printing of chemical names which suggest the need of more careful editing in future editions:

On page 53 we find "para-dimethyl-amino-benzaldehyde" but on page 373 "dimethyl-amino-benzaldehyde," "p-dimethyl-amino-benzaldehyde" and "p-dimethylamino-benzaldehyde"—all three versions within the space of six lines. Both "chromotropic acid" and "chromotrophic acid" are to be found on page 79. The adjective "colorimetric" is singled out, without apparent reason, for capitalization on page 81. Alphanaphthol and α-naphthol appear together on page 382, and tyrosine and tyrosin on page 407.

All in all this is an excellent book and will be found useful by clinical technicians, research assistants, and medical students.

Professor Koch passed away while this present edition was in press. The book testifies to his many years of work in biochemistry, to his excellence as a teacher, and to his insistence upon precision and meticulous care in laboratory technique.

OCCUPATIONAL MEDICINE AND INDUSTRIAL HYGIENE. By Rutherford T. Johnstone, A.B., M.D. Consultant in Industrial Health; Lecturer at the University of California, Los Angeles. Formerly Assistant Professor of Medicine, University of Pittsburgh School of Medicine. With One Hundred Seventeen Illustrations, Seven in Color. The C. V. Mosby Company. 1948.

As mechanization of our civilization has progressed, there has been a growing need for books describing and explaining the diseases arising from occupational exposures. Expanding knowledge of chemistry and physics has made possible the economical preparation of new materials and of new agents for processing familiar materials. Even in the home, strange compounds are becoming common: detergents are often not soaps. dishes are often not crockery, cleansing solvents not gasoline, adhesives not glue. In industry, not only manufacturing, but also agriculture and the service industries, the introduction of unfamiliar compounds is even more pronounced. Most of these novel materials are harmless, and in many instances they have been tested adequately to demonstrate this, but the practicing physician needs a better way of finding out which ones are potentially dangerous than by writing to *Queries and Minor Notes* of the J.A.M.A.

Moreover, California industrialists are becoming increasingly aware of the potential benefits of in-plant medical services. One factor retarding the greater utilization of medical knowledge by industry is the lack of preparation by physicians to take an effective, leading part in this endeavor.

In any attempt to cover this broad and changing field, the breadth and variety of topics to be considered is formidable. Previous authors have dealt with the problem by editing symposia or by very extensive quotations from various sources. This has almost inevitably led to imperfect balance of emphasis and lack of integration of the several contributions. Dr. Johnstone has written his own book, with the good result that each of its parts is well related to the whole. He has been free with his use of quotations, but he has made them part of his own work by discriminating choices and critical evaluation. The outcome is the best book ever written in this field. It is not a mere revision of Dr. Johnstone's previous work, *Occupational Diseases;* while retaining the best features of that book and bringing the material up to date, he has made a new and more effective approach to the problem of engendering understanding of occupational disease through more detailed and clearer explanations of the underlying processes by which noxious materials are taken into the body and absorbed, and the physiological and anatomical changes which result. He has added a section on industrial hygiene.

One of the best things about this work is the forthright, positive attitude of the author. He is not one to hedge about his opinions with ambiguous qualifications. Consequently, there are a number of points about which there is room for disagreement, but all the major premises are sound, and it is refreshing to read a medical text which reflects something of the author's personality.

The range of topics is from a broad consideration of the character of occupational medicine and industrial hygiene to detailed reports of cases of accidental intoxications. The opening chapters discuss the place of industrial medicine in the body of medical practice, the background of workmen's compensation laws and their relation to medical practice, and the importance of thorough study and accurate reporting in medicolegal cases. There is invaluable practical advice on the preparation of reports. After further generalizations on the functions of the industrial physician, the teaching of industrial medicine, the basic approach to a diagnosis of occupational disease, and a summary of useful laboratory procedures, the various noxious agents (solvents, metals, dusts, and so on) are treated categorically and individually. The nature of the agent, its uses, its effects in the body, the symptomatology, diagnosis, and treatment of poisoning are described and illustrated by appropriate case reports. Finally, after describing some industrial techniques of special interest, methods of protecting health of workmen, based on the materials covered before, are presented briefly, but sufficiently in detail to have practical value. There are many excellent illustrations, and several tabular summaries.

In all of this, especially in the case reports, the author's long and varied experience shows its value. There is no other book so likely to have the answers the doctor seeks when he must decide on the part played in an illness by the patient's work, or when he looks for methods of treatment and measures for protection from repeated exposure to occupational hazards.

PATHOLOGICAL HISTOLOGY. By Robertson F. Ogilvie, M.D., F.R.C.P. (Edin.), F.R.S.E., Lecturer in Pathology and Assistant in Forensic Medicine, University of Edinburgh, Third Edition with 260 Photomicrographs in Colour. The Williams and Wilkins Co. 1947.

Teachers of pathology agree that no perfect textbook on the subject exists, and this book is no exception. However, in the preface, the author specifically states that the book is designed to act as a companion to a standard textbook of pathology. In this respect, this book definitely fulfills its author's aims, and should be of considerable value to students of pathology.

For a complete understanding of morbid processes in tissues, the student needs detailed knowledge of the histologic changes occurring in various diseases. It is in this phase of the study of pathology that this book may assist the student in examination of sections under the microscope.

This third edition systematically considers in a text of 447 pages the pathologic lesions of most of the common disease processes. Each disease or pathologic lesion is defined briefly in an introductory paragraph, which includes a short discussion of factors of etiology, classification, and correlating clinical data. Then each lesion or process is described macroscopically and microscopically in a concise but thorough manner. These excellent descriptions are accompanied by 260 photomicrographs in color. To a pathologist and a photomicrographer they are well chosen, technically excellent and beautifully illustrate the descriptive text.

In only a few instances is the terminology different from that in most American textbooks, and these differences are not confusing. In the section on hepatic disease, the author's grouping of all types of cirrhosis under the heading "Common Cirrhosis," will be approved by few investigators in the field of hepatic disease and cirrhosis.

NURSING IN MODERN SOCIETY. By Mary Ella Chayer, R.N., M.A. Published by G. P. Putnam Sons, 1947. $4.00.

This publication includes three parts: Part One, The impact of social forces on nursing; Part Two, The influence of social forces upon community health needs; Part Three, Building a better future.

The reasons for the industrial revolution are discussed as are the relation of capital and labor, urban migration, family life, medical care under voluntary insurance plans and by compulsory governmental legislative action.

Nursing is described as a social force and legislation is advocated to insure its place as such. The program of the National Nursing Council is outlined, as is the organization of the Joint Committee on Auxiliary Nursing. Personnel policies on collective bargaining for nurses receive attention. Special consideration is given to the organization of various nursing bodies. Raymond Rich Associates have been employed as technical consultants to these bodies, to advise on details of organization of professional nurses and on the legal steps to be taken to accomplish their ends.

The view is expressed that nursing should be an autonomous profession and that this is the time to make it so. The professional nurse is considered the one to define properly the functions of medical social workers, physical therapists and practically all hospital personnel. Direction of various types of hospital personnel is seen as appropriately under the direction of the professional nurse rather than under the direction of medical staff or hospital superintendent. Recent surveys have shown the medical profession to be aware of such aims on the part of those in control of organized nursing—and to be aware also of a deterioration in the quality of the nursing care of the sick. The same surveys reveal agreement on the one hand that nurses are underpaid, and on the other that the cost of special nursing is prohibitive to the average patient, and agreement too that vocational nurses, after short periods of training, are able to furnish the care most needed by patients. The training of such a group in our nursing schools, however, is opposed by the central nursing organizations and in our private hospitals a closed shop prevails against practical nurses.

"Nursing in Modern Society" promotes the concept that the nurse is a social agent, and that she must organize and legislate. It expresses the aims of the central nursing bodies, dedicated to developing a profession independent of the medical profession, not an auxiliary to it. It advocates taking over many of the functions of the medical profession as well as independence from it.

We need another Florence Nightingale to redirect the trend of nursing. The heart seems to have gone out of it.

THE DISSECTION OF THE CAT (Felis Domestica)—A Laboratory Manual. By Bruce M. Harrison, Ph.D., Professor of Zoology and Head of the Department, The University of Southern California, Los Angeles, California. The C. V. Mosby Company, St. Louis. 1948. $3.50.

As the title of this manual suggests it is a laboratory outline for premedical students with good pen and ink drawings that are to be labeled by the student.

Some of the questions at the end of the chapters are on comparative anatomy. Three illustrations of the anatomy of man are used to compare with that dissected in the cat.

It should be an excellent guide for the premedical and prenursing student.

HANDBOOK OF FRACTURES. By Duncan Eve, Jr., M.D., F.A.C.S., Surgeon and Chief Nashville, Chattanooga and St. Louis Railroad. The C. V. Mosby Co., St. Louis. 1947. $5.00.

The handbook is an excellent portrayal of many years' experience and careful work on fractures by a man conversant with modern principles of fracture treatment. As such, it is valuable to the specialist in this field.

The author has expressed the hope that the handbook will be helpful "to the younger and more occasional worker in the field." The handbook would be of value to such a man, if he also has at his disposal a good two-volume treatise on

fractures. The fact remains that the less a doctor knows about a subject the more he needs to rely on books and the experiences of others.

INTRODUCTION TO HUMAN PHYSIOLOGY. By William D. Zoethout, Ph.D., Professor Emeritus of Physiology in the Chicago College of Dental Surgery (Loyola University). 138 Text Illustrations and 4 Color Plates. The C. V. Mosby Company, St. Louis, 1948. $4.00.

This book was designed for "the reader desirous of obtaining a fundamental knowledge of the operation of the human body but having no previous knowledge of the basic sciences of Physics and Chemistry." Like many books addressed to such an audience the present work is both elementary and superficial. Moreover some of the statements found in this book are clearly wrong. Thus on page 257 one finds the surprising and erroneous comment on insulin that, "It is now made synthetically; this greatly reduced its cost." As insulin is a protein and as no protein has yet been synthesized, this mistake implies either carelessness or serious lack of information. On page 48 the production of alcohol and carbon dioxide from glucose by yeast is attributed to *an* unorganized ferment. This process, as is well known, involves not one but a whole series of enzymes. The discussion on glycolysis (page 77) would lead the reader to consider lactic acid a key substance in carbohydrate degradation instead of the by-product which the work of Meyerhof and others has shown it to be. The book as a whole impresses the present reviewer as labored and uninspired. It cannot be recommended to any reader who desires a discussion of the fundamentals of physiology which is illuminated by intelligence and insight.

TEXTBOOK OF GYNECOLOGY. By Emil Novak, M.D., F.A.C.S., Assistant Professor of Gynecology, The Johns Hopkins Medical School; Third Edition. The Williams & Wilkins Company. 1948. $8.00.

While the Textbook of Gynecology by Emil Novak is designed primarily for the student and practitioner, a trained Gynecologist will enhance his knowledge tremendously if he reads this well planned third edition. Elimination of operative technique makes possible a comprehensive treatise of the entire subject in some 500 pages of written material. Original illustrations, as well as those borrowed from other authors, depict the lesions and further embellish the descriptive material. The color photography is outstanding.

The chapters on cancer, adenomyosis, myomas and diseases of the vulva are particularly valuable. To the reviewer they best exemplify Dr. Novak's ability to correlate, clarify and summarize a large amount of material without losing any important factors. If you have heard the author speak on these subjects, it brings to mind the pleasant, stimulating conversational style which few teachers possess.

In two short paragraphs the vaginal smear method of diagnosis is carefully evaluated and will give the practitioner an answer to the patient who comes for "the simple test of diagnosing cancer," as publicized by the lay press.

In the discussion of total versus supravaginal hysterectomy on page 322 I quote, "The long continued discussion as to the relative advantages and disadvantages of the two techniques has pretty well crystallized in the viewpoint that the total operation is the one of choice, and it should be selected unless there is present some contraindication imposed by the local conditions in the case of great obesity, unusually deep pelvis, fixation of the uterus by extensive pelvic endometriosis or pelvic inflammatory diseases, or by the surgical limitations of the operator. In my own work, something like 75 per cent of hysterectomies are of the total variety." This seems to summarize in a concise, critical and unbiased manner the opinion of Gynecologists of the present day.

For therapy, the chapter on the menopause and the general discussion of gynecological organotherapy should discourage physicians who resort to the use of "shots" for every conceivable alteration of menstrual function and the associated vasomotor symptoms.

This book is a monumental volume to the author's ability and should be available in every medical library, both public and private, worthy of the name.

MENTAL HEALTH, A Practical Guide to Disorders of the Mind. By John H. Ewen, F.R.C.P.E., D.P.M., Physician and Lecturer in Psychological Medicine, Westminster Hospital; Medical Superintendent, Springfield Mental Hospital, London; Formerly Examiner in Psychological Medicine, Royal College of Surgeons, England. With a Chapter on Special Treatments and Their Practical Technique, by C. Friedman, M.D., (Vienna), L.R.C.P.&S., Ed., Registrar and Tutor, Department of Psychological Medicine, St. Thomas's Hospital. Psychotherapist, The Tavistock Clinic. Medical Officer, Insulin Therapy Clinic, Springfield Mental Hospital. The Williams & Wilkins Company, Baltimore, 1947.

The authors have written along lines of a textbook on psychiatry, with much more emphasis upon the diagnosis and treatment of the psychotic states with which they have apparently had more experience. The young physician who is entering institutional psychiatric work will find it more useful than the doctor who would prefer more psychological insight into the emotional problems of the patients he sees in his everyday practice. Comparatively little space is given to the discussion of the psychoneuroses, and almost none to the general conceptions of psychosomatic medicine. The chapter on "Specialized Treatments and Their Technique" includes descriptions of electrical convulsion treatment, insulin therapy, malarial therapy, prefrontal leucotomy, continuous narcosis, and narco-analysis, and this is concisely written and, on the whole, quite adequate in presentation. The conditioned reflex treatment for chronic alcoholism might have been included here, but apparently this method has not achieved the popularity it has assumed in the United States.

More emphasis upon the psychodynamic formulation of psychological disorders would have helped to improve this text. Such a statement as "Emotional shock considered from the organic viewpoint is a form of auto-intoxication and may produce the same effects on the mental life as the organic shock resulting from fevers and poisons" needs further elaboration. The author considers lactation an "exhaustive state," and the psychoses occurring during and after pregnancy as "organic reaction types of mental disorder," although he states "possible psychogenic factors must receive adequate consideration." This is still a controversial problem, but there is accumulating a large body of evidence indicating that psychological factors play a considerable role in the mental illnesses associated with pregnancy and the post-partum period. Most authorities would disagree with the author's statement that "epilepsy considered from the mental point of view is a progressive disorder culminating in terminal dementia." This might be true of some of the institutionalized epileptics, but these constitute only a small percentage of the large group of extramural epileptics. Such a fatalistic point of view would deter therapy which would prove so useful in this disorder. The section on "Legal Aspects of Mental Disorder" refers primarily to British law, much of which is not relevant to the practical problems with which the physician must deal in this country, although there is much of a general character in the principles laid down which could prove useful to the reader.

This book cannot be recommended as providing an adequate description on modern concepts in psychiatry because of its lack of presentation of the details of psychodynamic formulations of emotional problems.

MEDICAL JURISPRUDENCE

PEART, BARATY & HASSARD *of the California Bar*

A recent decision by the California District Court of Appeal (85 A.C.A. 251, May 7, 1948) involving a discussion of the doctrine of *res ipsa loquitur* may be of interest to physicians and surgeons.

The District Court of Appeals had before it a case arising from the following facts: At the trial the plaintiff patient testified that she had been suffering from a varicose vein condition in both legs from her thighs to her ankles. The defendant doctor made a visual examination of the patient and directed that she enter a hospital. While in the hospital the physician examined patient's legs again and then directed a hospital nurse to bring him a small basin of water and a silver nitrate pencil. The physician then dipped the pencil into the water and outlined the patient's leg veins that were to be removed. There were four of such markings made on each leg, two above the knees and two below. The plaintiff patient testified that shortly thereafter her legs began to burn and became very inflamed around the areas marked by the defendant, and that in a short time blisters formed at such areas. The defendant physician was unable to operate the next morning as had been planned, and upon examination of the patient's legs told her that the operation could not be performed because the burns were too severe. As a result of these burns, the plaintiff testified, she was forced to remain away from work and had to wear bandages for over a month, and she testified that she was still scarred from the burns.

The only other witness was the defendant physician himself, who testified that in his city it was the common practice of physicians in this type of operation to mark off with a silver nitrate solution the area to be operated upon, and that it was also standard practice in his area to mark off the operating area without first making any tests. He stated that prior to his treatment of plaintiff he had performed three or four hundred of such operations and that everything he did in this case was performed according to the ordinary standards of practice of surgeons in his city.

On this evidence the trial court granted the defendant physician's motion for a non suit on the ground that the plaintiff had failed to show that the defendant physician did not possess and use the degree of skill possessed by other practitioners in the same locality.

On appeal the District Court of Appeal stated that the trial court was correct in granting the non suit unless the doctrine of *res ipsa loquitur* was applicable.

In its opinion the court stated that the doctrine normally applies where the accident that occurred was such that in the ordinary course of events the defendant using ordinary care, it would not have happened, and where the instrumentality causing the accident was under the control of the defendant. In an analysis the District Court of Appeal held that all of the requirements of this doctrine had been met and therefore this operated to raise an inference of negligence and the trial court, it stated, should not have granted the non suit.

It may be noted in this opinion that a dissent was entered by one of the Justices of the District Court of Appeal in which he stated that negligence upon the part of a physician or surgeon is not presumed from the mere happening of an injury to a patient under his care. Further, that the doctrine of *res ipsa loquitur* should not be extended to the point where negligence from the mere happening of an injury to a patient might be presumed. In his analysis the dissenting Justice states clearly that the law has never held a physician or surgeon liable for any untoward result which may occur in medical practice. It requires only that he shall have the degree of learning and skill ordinarily possessed by physicians of good standing practicing in the same locality, and that he shall use the ordinary care and diligence in applying that learning and skill to the treatment of his patients. From this the dissenting Judge concluded that the facts did not warrant the application of the doctrine of *res ipsa loquitur* and, therefore, the judgment by the lower court should have been upheld.

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Hay Fever	790 CASES	304 (38%)	234 (30%)	252 (32%)
Asthma	397 CASES	119 (30%)	82 (21%)	196 (49%)
Pollen Asthma	226 CASES	73 (32%)	55 (24%)	98 (44%)
Vasomotor Rhinitis	130 CASES	20 (16%)	42 (32%)	68 (52%)
Urticaria	24 CASES	4 (17%)	8 (33%)	12 (50%)
Eczema	3 CASES			3
TOTAL	1,570 CASES			

Side Reactions

No Reactions 126 Cases (8%)
Moderate Reactions . . . 314 Cases (20%)
Severe Reactions 1,219 Cases (72%)

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VENEREAL DISEASES IN SAN FRANCISCO—1940-1947

The San Francisco Department of Public Health has prepared the following tabulation on reported incidence of venereal diseases in San Francisco over the past eight years. Although the armed forces were found in the local population prior to 1944, no segregation of civilian and military cases was made until that year.

Except for slight fluctuation that may be accounted for by the entrance into the community of war activities, no significant differences occur over the eight year period. Therefore, the problem of venereal diseases has not been solved in this community, the Health Department says.

A very definite downward trend is noted in death rates for syphilis, but some of this may be due to the higher population estimates used in computing the rates and also to the fact that through these particular years the population increment was largely in the younger age groups, says the Department's report.

The definite upward trend in the reported incidence of gonorrhea, according to the Department of Health, is probably due not only to this younger age group in the population but also to the changes in population distribution.

Syphilis Cases

Year	Civilian	Military	Total Deaths	Death Rate per 100,000
1940	2494		138	21.8
1941	2426		140	22.1
1942	3002		117	16.1
1943	2987		161	20.8
1944	2721	294	109	14.1
1945	3153	383	91	10.7
1946	2748	603	79	9.5
1947	2540	261	75	8.6

Gonorrhea Cases

Year	Civilian	Military
1940	2634	
1941	1974	
1942	2795	
1943	2171	
1944	2446	2308
1945	3892	3434
1946	4505	2604
1947	4341	1058

PULMONARY TUBERCULOSIS IN SAN FRANCISCO—1947

During 1947 there were 316 deaths from pulmonary tuberculosis in San Francisco with a rate of 36.1 per 100,000 population, the San Francisco Department of Public Health reports. This compares with 349 deaths and a rate of 42.2 for 1946. Compared with 1937 (ten years ago) the reduction is even more striking as the number of deaths then was 398 with a rate of 57.4. This is actually a 37 per cent decrease in the death rate for the ten-year period.

There were 1027 cases of pulmonary tuberculosis reported during 1947. This exceeded the number of 1946 by 128; and 1946 in turn exceeded 1945 by 87 cases. This increase is caused at least in part by the

(Continued on Page 36)



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PULMONARY TUBERCULOSIS IN SAN FRANCISCO—1947

(Continued from Page 34)

case-finding program initiated by the San Francisco Department of Public Health and the San Francisco Tuberculosis Association. During 1947, 87,248 persons were given X-ray examinations through facilities made available by this program. The number for 1946 was 62,367.

The increasing negro population (4846 in 1940 and 55,000 estimated in 1947) is another factor to be considered in evaluating the increase in incidence. The above table shows a rate for negroes almost double that for whites. The Chinese rate is almost double that of the negroes but the Chinese population is more stable (18,000 for 1940 and 20,000 for 1947).

RACE—PULMONARY TUBERCULOSIS

	1947		1946	
	Cases	Rates	Cases	Rates
White	791	100	679	88
Negro	100	182	75	234
Chinese	96	480	78	433
Japanese	15		8	
Filipino	21		2	
Other	4		7	
Totals	1,027	117	849	103



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TULAREMIA INCREASE REPORTED IN OZARKS REGION

Tularemia, or rabbit fever, is on the increase in the Ozark Mountain region, three physicians report in a recent issue of *The Journal of the American Medical Association.*

Authors of the report are Lieut. (jg) Roger B. Bost, M.C., United States Naval Reserve, Capt. S. C. Percefull, M.C., United States Army and Howell E. Leming, M.D., all of Fayetteville, Ark.

According to the article, seven cases of tularemia were recorded from 1936 to 1940. From 1941 to 1944, nine cases were seen, and from 1945 to date, 38 cases have been treated. Twenty cases have been seen thus far this year.

"In contrast with statements concerning the usual sources of the disease," the article says, "it has been observed here that the source of the disease in 63 per cent of these cases was tick bites; in 14 per cent it was contact with rabbits, and in 4 per cent contact with squirrels."

Many authorities give rabbits as the main cause of tularemia, some reporting that 90 per cent of all cases of the disease come from contact with these rodents.

Analyzing 54 cases of tularemia in the Ozarks region, the physicians report successful use of streptomycin in its treatment. Using this antibiotic in 27 of the 54 cases, they were able to reduce the mortality rate to zero, in contrast to a rate of 14 per cent incurred in the 27 cases in which streptomycin was not used.

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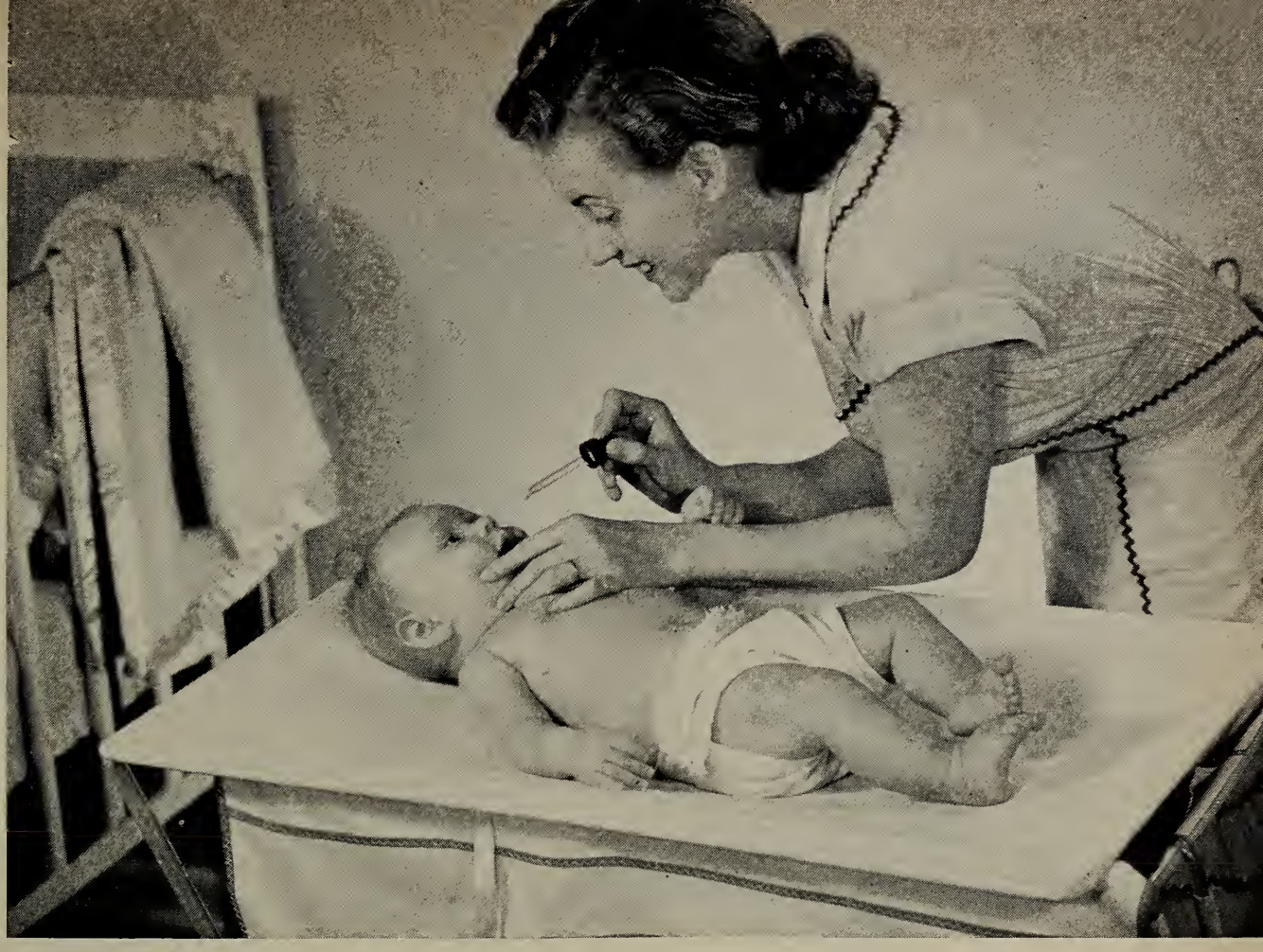
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WOMEN PAST 49 RESPOND BEST TO TREATMENT FOR CANCER OF CERVIX

Women past 49 respond more favorably to treatment for cancer of the cervix than do younger women, two physicians of the Mayo Clinic, Rochester, Minn., have found in a study made of 3,798 patients at the clinic from 1915 through 1944.

Writing in a recent issue of *The Journal of the American Medical Association*, the physicians—Harry H. Bowing and Robert E. Fricke—say that "the patient more than 49 years of age has a definitely favorable factor influencing the five year cure rate."

Women 49 or older responded better to all types of treatment except that younger women were more able to withstand the effects of surgery.

Twenty-nine per cent of the women between the ages of 30 and 49 who were treated before 1940 and who were traced by the physicians were living five or more years after leaving the hospital. In the 40 to 69 group, nearly 37 per cent were living five or more years after leaving the hospital.

The majority of patients with cancer of the cervix are in the menopausal years of their lives, the study shows. About two-thirds of the entire group were from 40 to 59 years of age and only a few patients were under 30 or over 69.

The importance of early treatment, systematic examination after treatment, individualized therapy, and the harmful effects of treatment by inadequate methods were also emphasized in the study.

Seven types of treatment were used, the type being determined by the stage of the disease, the patient's condition and previous treatment, and other factors:

(1) Radium therapy (2) Roentgen therapy (3) Surgery (4) Surgery, radium therapy, and roentgen therapy (5) Combined radium therapy and roentgen therapy (6) Surgery and radium therapy, and (7) Surgery and roentgen therapy.

Combined methods are often more successful than any method used alone, the study points out.

The importance of early treatment is shown by the fact that among the patients at the clinic from 1915 through 1939, 65 per cent of those treated in an early stage of the disease and who were traced by the physicians were living five years after leaving the clinic.

Emphasizing the importance of systematic examination after treatment, the physicians say:

"The importance of a well-planned follow-up system cannot be overstressed. We recommend reexamination every three or four months for the first post-treatment year; every six months for the second post-treatment year; and every year thereafter."

Stressing the adaptation of therapy to the needs of the individual patients, the physicians comment:

"It seems reasonable that by a combination of selected methods in proper sequence the most good can be obtained for the patient. So far, there are no mass production procedures that will effectively control the malignant disease."



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DOCTORS SAY BONE BANK HAS GREAT POSSIBILITIES

Bone preserved in a frozen state for weeks is of "definite value" in bone-grafting operations, Dr. Leonard F. Bush, Danville, Pa., and Dr. C. Zent Garber, of New York, write in a recent issue of *The Journal of the American Medical Association.*

In an article entitled "The Bone Bank," the two doctors say that "if foods, serums and other perishable substances could be kept in a low temperature freezing cabinet, we decided that perhaps this method could be used to preserve bone so that a constant supply would be available at all times."

Experiments were undertaken and it was found that human bone can be preserved apparently indefinitely in a freezer at minus 20 to 30 centigrade.

"Spinal fusions for scoliosis and disorders in the lower part of the back, the filling of large bone cysts and the replacement of defects in bone are a few of the common problems in which large quantities of bone are necessary," the doctors state in their article.

The doctors, in their experiments, used large chinchilla rabbits. Control studies were made. Thirty-two bone transplantations were made by 28 operations on 19 animals. There were no casualties and in only one wound was there a superficial infection.

The experimental bone-grafting studies on rabbits showed that freezing at low temperature is a safe method of prolonged preservation of bone for grafting purposes. Bone grafts three to six weeks after im-

(Continued on Page 18)

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Recent evidence[1,2] indicates that the presence of fat in a mixed dietary considerably decreases the specific dynamic effect of the three basic nutrients, thus promoting optimal utilization of the protein ingested.

This survey of the nutritional significance of fat again emphasizes the valuable role of meat fat in the daily dietary.

[1] Forbes, E. B., and Swift, R. W.: J. Nutrition 27:453 (June) 1944. [2] Forbes, E. B.; Swift, R. W.; Elliott, R. F., and James, W. H.: J. Nutrition 31:203;213 (Feb.) 1946.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.

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DOCTORS SAY BONE BANK HAS GREAT POSSIBILITIES

(Continued from Page 14)

plantation proved successful. Some of the bone used had been frozen from 28 to 84 days.

"Having proved that this method of preserving bone was successful in animals, we felt it was safe to attempt it in man," the article says. "Thus all available clean fresh bone was placed in bottles and frozen at minus 25 degrees centigrade. Because infection developed in one case, the bone is now kept for two weeks before using, while the donor remains under observation for evidence of developing wound infection."

The doctors explained that by "exercise of diligence," considerable bone may be accumulated from many sources.

In discussing the clinical results, the doctors state that homogenous bone has been used in 126 operations in 104 patients. "Of these, 24 operations were by direct transfer; refrigeration at plus 2 to plus 5 C. was used in 37 instances, and the bone was stored in deep freezer for 43 operations."

In the 104 cases in which donor bone was used, there were only four complications. "The donor bone," the article says, "furnished a framework for the formation of new bone by substitution and by furnishing the necessary calcium for this new bone."

In discussing the paper, Dr. J. R. Cobb says that from his experience at the Hospital For Special Surgery in New York bone can be kept indefinitely if it is kept constantly at a sufficiently low temperature without contamination and sealed.

(Continued on Page 22)

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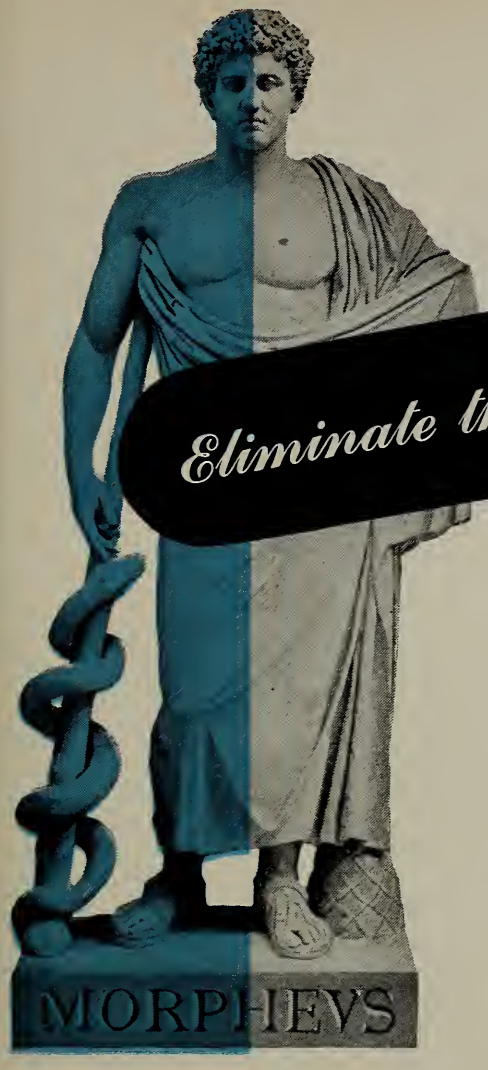
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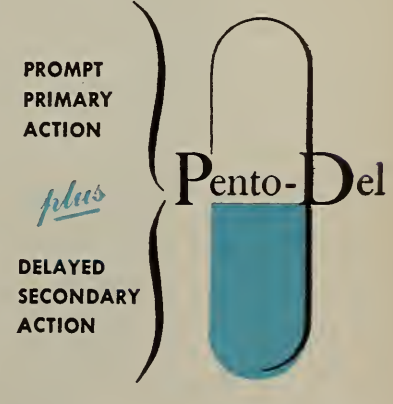
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1. Kasper, J. A. and Jeffrey, I. A.: A Simplified Benedict Test for Glycosuria, Amer. J. Clin. Pathology, *14*:117-21 (Nov.) 1944.

2. Haid, W. H.: The Use of Screening Tests in the Clinical Laboratory, J. Amer. Med. Tech., *8*:606-14 (Sept.) 1947.

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LISTS 6 RULES TO GUARD CHILDREN AGAINST POLIO

Despite the lack of a definite preventive for infantile paralysis, parents may guard their children this summer by following a few simple rules, Dr. Hart E. Van Riper, of New York, says in the current issue of *Hygeia*, the health magazine of the American Medical Association.

Dr. Van Riper is medical director of the National Foundation for Infantile Paralysis and at one time served as a resident in pediatrics at Children's Hospital in Cincinnati. He has been connected with the National Foundation since 1945.

Dr. Van Riper listed these safeguards:

1. Practice cleanliness.
2. Avoid new contacts.
3. Don't get overtired.
4. Avoid chilling.
5. Don't swim in polluted waters.
6. Call your doctor at once.

"These are simple safeguards, but important: especially the advice to call your doctor at the first suspicious signs. Early medical attention is the best protection parents have against infantile paralysis," Dr. Van Riper's article says, adding:

"An answer to the question of where infantile paralysis will strike this summer cannot be wholly relied upon. From studying the visitations of previous epidemics, it is evident that infantile paralysis moves in cycles with a four to six year lapse between epidemics.

"In attempting to guess where infantile paralysis may strike in this summer of 1948, we can see that the states along the Atlantic Coast, from South Carolina northward, have been relatively free from epidemics of infantile paralysis for the past four to six years. It is possible then, that the states along the Atlantic seaboard, from South Carolina to Maine, may experience a resurgence of virus activity.

"But whether outbreaks will actually take place and how severe they will be, no one can be certain. Nor should there be any undue alarm in the areas named. All efforts have been made to safeguard these potential trouble areas.

"Severe infantile paralysis epidemics once seemed to be a problem peculiar to the American people and a few of the nations of Europe. Today infantile paralysis is considered a dangerous world health problem. The virus is evidently free from climatic restrictions. Cuba as well as Iceland has recently experienced epidemics. Nor has geographic remoteness been a barrier to the disease.

"Many foreign countries face infantile paralysis as a new health problem. It is to our interest as well as theirs that the knowledge we have laboriously accumulated be shared with them and that they in turn acquaint us with their experiences.

"It is for this purpose that the National Foundation for Infantile Paralysis is sponsoring the First International Poliomyelitis Conference to be held at the Waldorf-Astoria Hotel in New York City next week, beginning July 12.

"There is one problem which should take precedence over all others—'What is infantile paralysis?'

(Continued on Page 22)

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SIMILAC *Similar to breast milk*

DOCTORS SAY BONE BANK HAS GREAT POSSIBILITIES

(Continued from Page 18)

"All of us who have used refrigerated bone," he says, "have been impressed by the simplicity, safety and usefulness of the bone bank. However, while a bone bank on a small scale is desirable in every hospital with an active bone and joint service, there are great potentialities for further development of the bone bank. We need an organization on a much larger scale, of a community bone bank to supply the needs of surgeons for bone transplants of every size and description."

LISTS 6 RULES TO GUARD CHILDREN AGAINST POLIO

(Continued from Page 20)

We may be fighting not one disease, but a whole family of only slightly related diseases.

"We do know already that there are many strains of infantile paralysis virus capable of producing the clinical symptoms. But we don't know how closely related these virus strains are, or, indeed, if they are biologically related at all; and we do not know whether special measures of prevention or treatment are necessary for each individual type.



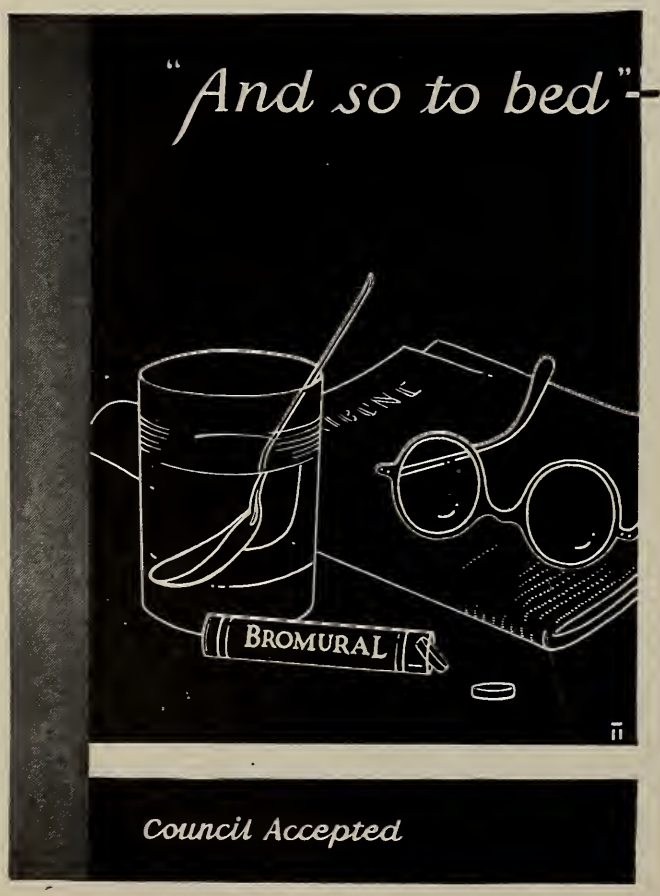
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PREPARE GLOSSARY OF TERMS USED IN ATOMIC ENERGY

To better inform the physician, the Council on Physical Medicine of the American Medical Association has prepared a glossary of terms used in atomic energy and nuclear physics.

The introduction to the pamphlet says that "nuclear physics as it develops will have important consequences to the practicing physician. New types of injury may require treatment, new hazards will require prevention and new methods of treatment, diagnosis, and research will be introduced. In attempting to inform himself about recent discoveries the physician is constantly baffled by the new vocabulary, which contains some words too recent or too technical to be found in older or less specialized dictionaries. The present glossary is intended to be helpful in this respect.

The glossary was adopted by the Council on Physical Medicine of the American Medical Association, assisted by a large number of consultants on roentgen rays and radium and on the medical aspects of atomic energy.

The glossary explains such terms as atom, atomic number, chain reaction, cosmic rays, cyclotron, element, energy, isotron, isotopes, neutron, radioactivity, radioactive chain, radon, plutonium, uranium, volt and wavelength.

The pamphlet also contains symbols used in writing nuclear reactions.



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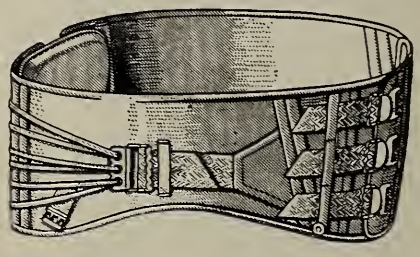
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The Response of Articular Cartilage to Trauma

With Special Reference to the Knee Joint

KEENE O. HALDEMAN, M.D., and RALPH SOTO-HALL, M.D., *San Francisco*

TRAUMATIC and degenerative changes in the articular cartilages have often been overlooked and emphasis has been placed upon injuries to the bones because the roentgenogram clearly demonstrates the latter lesions but gives little clue to the state of the cartilage. The surgeon is impressed by the degree of alteration seen in the cartilage of the exposed joint, the roentgenogram of which has been normal. It is these articular lesions which are often the greatest cause of disability, particularly following fractures which occur in the vicinity of joints. They may also be a cause of prolonged disability following contusions and sprains. The high frequency of such a condition as chondromalacia of the patella in minor injuries of the knee is well indicated by a study of 289 consecutive arthrotomies of the knee, made in three separate military hospitals.[7] In this series, 10 per cent showed degenerative changes in the articular surface of the patella.

King[4] has shown experimentally in dogs that such changes occur in the articular surfaces of the knee three or four months after the excision of a part of the medial semilunar cartilage. Other experimentation[5] has shown that the division of the medial collateral and crucial ligaments, by allowing relaxation of the knee, will produce severe articular lesions. Such clinical and experimental observations explain the persistent symptoms which may follow the excision of a semilunar cartilage, or other arthrotomy of the knee. Similar lesions involving the cartilage of the lower end of the humerus often follow fractures of the head of the radius.

Articular cartilage is a highly specialized type of connective tissue which has the main function of providing a smooth gliding surface for the end or side of a bone. The method of nutrition of this cartilage is not clearly understood. Probably the basal layer of cartilage is supplied by the blood vessels of the underlying bone, whereas the more superficial cartilage cells are nourished chiefly by synovial fluid, since no capillaries can be demonstrated. This synovial fluid is probably diffused through the cartilage by the actual pressure and contact of the articular surfaces. Two hundred years ago the famous anatomist, William Hunter,[3] remarked, "If we consult the standard Chirurgical writers from Hippocrates down to the present age, we shall find, that an ulcerated cartilage is universally allowed to be a very troublesome disease; that it admits of a cure with more difficulty than a carious bone; and that, when destroyed, it is never recovered. Hildamus, in considering these diseases, has observed, that when the cartilages of a joint were destroyed the bones commonly threw out a cementing callus; and thus a boney anchylosis, or immovable continuity, was formed where the movable joint had been. So far as I have had opportunities of examining diseased joints, either after death or amputation, I have found, according to the nature and stage of the disease, the cartilages in some parts reddish and lax; or soft and spongie; or raised up in blisters from the bone; or quite eroded, and, perhaps, the extremities of the bones carious; or, lastly, a boney anchylosis formed. But I could never see, nor indeed hear of, the least appearance of an exfoliation from the surface of the cartilage." The same author described the circulus articuli vasculosus which is thought to supply nourishment to the peripheral portion of the articular cartilage through its perichondrium. It has been suggested[1] that this peripheral zone of cartilage has greater power to repair than the central area, a

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finding which we have frequently encountered in the patella. However, Shands[6] has failed to demonstrate this difference experimentally.

Because of the highly specialized nature of cartilage, there is very little power of regeneration. The response often varies with the depth and severity of the injury sustained. Damage to its superficial layers results in fibrillary changes which gradually extend in area and depth until a large area of chondromalacia is formed. Fractures and operative procedures which produce lesions extending entirely through the articular cartilage into subchondral bone are followed by a proliferation of connective tissues which, after a long period, undergoes metaplasia into a type of fibrocartilage which may provide a fairly satisfactory gliding surface. We have studied these reparative processes experimentally in rabbits by the production of closed fractures into joints and by the removal of small segments of articular cartilage and bone from the lateral condyle of the humerus.[2] The results of this work are in agreement with the observations of others to the effect that hyaline cartilage repairs injuries very slowly and incompletely through the formation of connective tissue which is gradually transformed into fibrocartilage and rarely into hyaline cartilage.

Another approach to this problem has included the microscopic study of surgical specimens from humans removed from 28 joints at various intervals following fractures which involved these joints.[2] This series included the head of the radius (five cases), carpal navicular (five cases), carpal lunate (four cases) and femoral condyle (three cases). Here also one observes little if any regeneration of articular cartilage following injury although the underlying bone heals quite rapidly. Figure 1 shows a microscopic section of a part of the articular surface of a navicular bone which was excised one year after sustaining a fracture which did not unite. The complete absence of any effort at repair is seen in the cleft which extends through all layers of articular cartilage but does not, in this area, continue into the subchondral bone.

The main lesions which are found clinically to involve cartilage are the following:

1. Chondromalacia,[8] which is most often seen in the patella but which may also occur in the femoral condyle and in the capitellum of the humerus. It is found after minor injuries such as strains and contusions. Its appearance some weeks or months after the injury suggests that it is associated with some impairment of nutrition of the cartilage. Although this condition may occur at any age it is more prevalent in young people. Certain individuals seem predisposed to its development. Another cause of chondromalacia is an instability or subluxation of the patella which subjects the knee joint to repeated minor traumata.

2. Osteochondritis dissecans, a condition which may be due to the occlusion of a terminal artery in subchondral bone, and which is often found in young individuals.

3. Degeneration of articular cartilage which is secondary to such internal derangements as tears of the semilunar cartilages, osteochondritis dissecans or osteochondromatous loose bodies.

4. Fractures extending into a joint.

5. Aseptic necrosis as is seen most often in the head of a femur following fracture (Figure 2) and in the proximal fragment of a fractured carpal navicular.

6. Degenerative changes in cartilage resulting from improper weight bearing which may be seen in overweight individuals with genu valgum.

The underlying causes of articular degeneration can be divided into five main groups:

1. Impairment of blood supply. This is the ob-



Figure 1.—Chondral fracture of carpal navicular 1 year after injury. A. Articular cartilage. B. Subchondral bone. C. Cleft in cartilage.

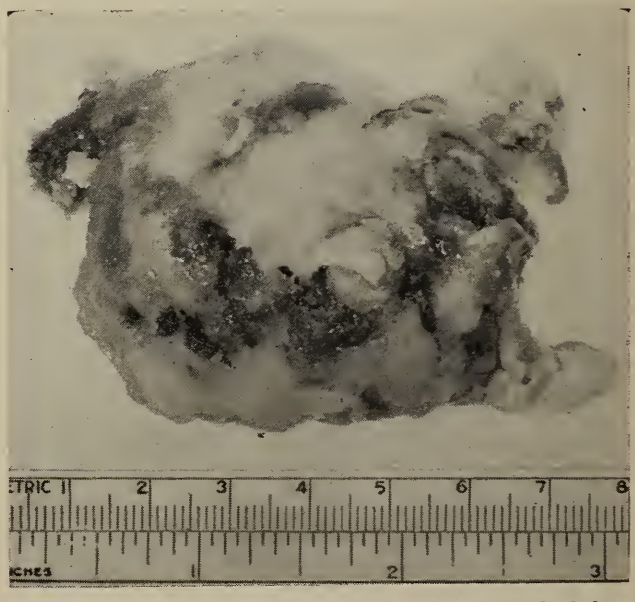


Figure 2.—Articular surface of head of femur which has undergone aseptic necrosis following fracture of femoral neck.

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2. Damage to the basal layer of cartilage as seen in complete fractures or in osteochondral fractures.

3. Friction of irregular opposing joint surfaces. This factor comes into play with improper reduction of a fracture or in a lesion of an articular surface which results in a similar degenerative area in the opposing surface. This is well illustrated by the "mirror image" lesions of the femoral condyle following chondromalacia of the patella. Figure 3 shows an example of osteochondral fracture of the patella with detachment of about one-half of its articular surface and the production of a similar area of destruction in the opposing femoral condyle. The normal pressure and gliding mechanism of each surface is necessary for the health and nutrition of the opposite side.

4. Failure of functional contact of the articular surface. This is seen in unreduced dislocations of the head of the humerus or radius. In such cases, with varying degrees of rapidity, there is a progressive loss of the smooth articular surface which becomes pitted or may be invaded by connective tissue. The occasional speed of this process emphasizes the seriousness of delay in the reduction of a dislocation and the futility of the attempt to obtain a normal joint in a dislocation of long duration.

5. The large group of arthritis of pyogenic or rheumatoid origin is mentioned for the sake of completeness but is not covered in this presentation.

Prevention was never of greater importance than in the handling of injuries to articular cartilage. Such prevention depends upon early diagnosis and operative treatment of internal derangements of joints. A long period of hesitation or conservative treatment in the presence of an obvious loose body or tear of a semilunar cartilage often leads to secondary changes in the articular surfaces which produce residual symptoms and even permanent disability. Thus, decision as to operation must not be delayed too long. Any deformity of the weight-bearing axis, either developmental or traumatic, must be corrected to avoid improper stresses on joints. Overweight often leads to increased joint trauma, particularly in the knee. The role of the chronically subluxating patella in the causation of lesions of the femoral condyle should be recognized. This condition should be corrected, as an unstable patella will lead, after a number of years, to a disabling patello-femoral arthritis.

During operation special care should be taken to avoid any trauma to articular surfaces such as might be caused by the careless use of retractors or sponges. The rapid restoration of function by early postoperative mobilization of joints is good insurance against prolonged disability. During the period of splinting of joints, functional treatment by quadriceps setting exercises or by free movement of the fingers is indicated in order to preserve circulation and the free movement of tendons in the region of the articulation and to prevent atrophy of muscles. This explains the good results which are obtained in Colles fractures and other injuries when activity of the adjacent muscles is maintained throughout the period of immobilization.



Figure 3.—Operative exposure of knee joint in which an osteochondral fracture of the patella has resulted in the detachment of a loose body of cartilage, and in the formation of a mirror image lesion in the femoral condyle. P. Patella. L. Loose Body. F. Articular surface of femur.

From what has been said it is obvious that a major factor in the prevention of prolonged or permanent disability is the perfect reduction of fractures which involve joint surfaces. No percentage of error is allowable as any irregularity leads to chronic irritation and permanent damage. It is for this reason that articular fractures in such weight bearing joints as the ankle, with its close fitting mortise, frequently are best treated by open reduction, perfect apposition and internal fixation of the fragments.

Although at operation on a chronically disabled joint one may be amazed by an advanced degeneration of its cartilage, he should not lose hope of being able to better the condition, for in some cases brilliant results in relieving pain and increasing function are attained. Magnuson,[5] describing joint debridement, has shown that the removal of exostoses and involved cartilage, accompanied in some instances by partial synovectomy, has brought about a great improvement in the function of joints. We have used this operation frequently and, in the presence of exposed subchondral bone, have in addition placed multiple drill holes in the sclerotic part of the bone in the hope of encouraging the formation of granulation tissue which should eventually be converted into a type of fibrocartilage. In certain circumstances it is possible to eliminate pain by the removal of one of the components of a damaged joint. Examples of

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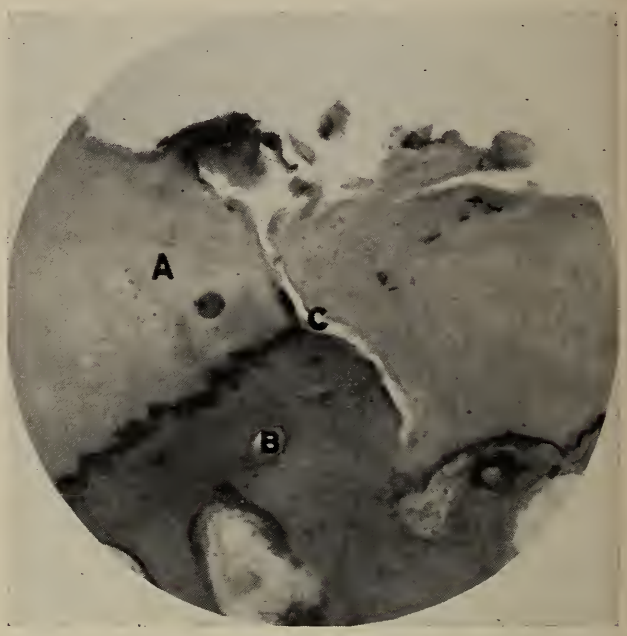


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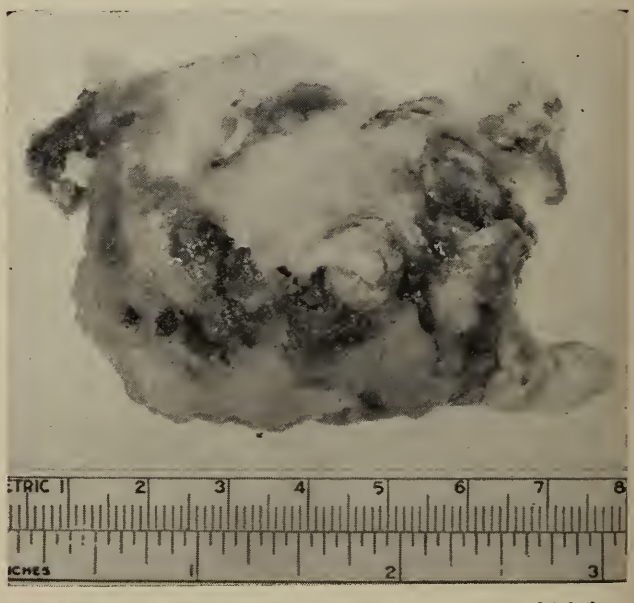


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such instances include the excisions of the patella, head of the radius, outer end of the clavicle and lower end of the ulna. All of these procedures have had adequate trial and offer a great help in correcting these mechanical derangements of joints.

Finally, in weight bearing joints, when such conservative procedures as those described above are not feasible, and in cases of extensive degeneration, arthroplasty or arthrodesis is available. These two procedures have definite application and should be chosen with great care with regard to the ultimate function of the part. An arthroplasty is often entirely adequate in those individuals employed in sedentary and clerical work, whereas in those employed in more laborious ocupations, an arthrodesis will be more satisfactory.

SUMMARY

Hyaline cartilage is a highly specialized connective tissue with very little power of regeneration. An understanding of its response to injury explains many of the disabilities which follow trauma. Lesions of articular cartilage are amenable to surgical treatment with a high proportion of good results.

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The Anti-Shock Action of Sodium

H. C. Bergman, Ph.D., and Myron Prinzmetal, M.D., *Los Angeles*

RECENT reports have demonstrated the efficacy of sodium salt solutions in lessening the mortality from experimentally induced shock. This literature has been reviewed by Rosenthal and Tabor[11] who concluded that the combined effects of fluid loss, sodium loss and potassium toxicity influenced mortality in shock.

With a radioactive sodium tracer, Fox and Keston[4] showed that there is a large accumulation of sodium in injured tissues along with reduction in plasma volume. They found that treatment with isotonic saline approximating one-half the extracellular volume restored the plasma volume.

It is generally agreed that the circulating blood volume is reduced in shock. Depending upon the nature of the trauma, the reduction in circulating blood volume occurs by local fluid loss[2] and by hyperemia (due to capillary atony) leading to retention of blood in viscera.[5]

It was shown that vascular congestion is caused by a toxic factor which was demonstrated in the blood of shocked animals by transfusion[6] and by renal perfusion experiments.[7] Insofar as local loss of fluid is concerned, the therapeutic use of large volumes of isotonic sodium chloride solution would hardly be expected to reduce loss of fluid into an injured region. Therefore, a study was made on the influence of sodium chloride on the vascular congestion observed in shock. In this report the effect of therapeutic amounts of isotonic sodium chloride solution was studied on changes in circulatory volume and on the vascular congestion of some of the organs of mice subjected to thermal injury.

All the experiments were performed with Swiss mice (18 to 26 gm.) equally distributed in groups as to weight and sex. Details of the scalding method for production of thermal injury have been described elsewhere.[8] Bleeding volume (the amount of blood obtained by rapid exsanguination) as a per cent of the body weight was determined in mice anesthetized with ether, by opening the thorax, removing the heart and mopping up the blood with weighed cotton pledgets.[6]

The method for estimating the relative hemoglobin retention of tissues from shocked, exsanguinated mice is described in another report.[1] The amount of hemoglobin retention in the exsanguinated liver was taken as an index of the degree of vascular congestion.[6] In the experiments reported here, ten pooled livers per group were examined and the average of five such groups is shown in Table 1. Each value was corrected for hemoconcentration based on hematocrit measurements. The values are reported as the per cent of retained hemoglobin compared with the hemoglobin content of exsanguinated normal livers taken as 100 per cent.

For the production of thermal injury, both hind limbs of each of 150 mice anesthetized with ether were immersed in water at 100° C., for 20 seconds. Thirty minutes later, a volume of 0.85 per cent sodium chloride solution equivalent to 5 per cent of the body weight was administered by stomach tube to 50 of these mice. Another 50 mice received similar amounts of distilled water. The remaining 50 mice were untreated. From 2.5 to 4.5 hours after the burn, the animals, anesthetized with ether, were bled, and the livers removed. At this time, an additional 50 unburned mice were bled and the livers removed to provide a control group of normal animals.

In another experiment, for comparison with the preceding series, 90 mice not subjected to trauma were divided into three groups of 30 mice each. One group received by stomach tube a volume of isotonic saline equal to 5 per cent of the body weight, a second group received a similar volume of distilled water and a third group remained untreated. All three groups of mice were bled two to four hours after starting the experiment.

The results are summarized in Table 1. In agreement with previous work a significant reduction was found in the bleeding volume of burned mice. The bleeding volume of the saline-treated mice was statistically significantly greater than that of the non-treated burned mice. On the other hand, similar amounts of distilled water did not significantly alter the bleeding volume of burned mice. In a second series of experiments with mice not subjected to trauma, isotonic saline, but not distilled water, again significantly increased the bleeding volume. Thus it would appear that sodium salts are necessary for retention of enough fluid to increase blood volume.

In Table 1, the retention of liver hemoglobin is compared in exsanguinated burned mice and exsanguinated non-traumatized mice. It is evident that sodium chloride solution decreased the amount of hemoglobin retained in the livers of burned mice.

Thus it appears that the increased bleeding volume of burned mice, following the administration of isotonic saline, can be due to the decreased retention of blood in the capillary bed. That a toxic factor is responsible for promoting the sequestration of blood by causing capillary atony was demonstrated in previous work.[6, 7] The mechanism whereby sodium causes a decrease in capillary atony is unknown.

The fact that isotonic saline, but not distilled water, increased the bleeding volume of normal mice shows that the sodium chloride aids the retention of fluid in the circulation. Warren, Merrill and Stead[13] have injected physiologic saline in amounts as high as 50 to 100 per cent of the body weight into dogs subjected to tourniquet shock. This infusion maintained the circulation at a normal level but there was

From the Institute for Medical Research, Cedars of Lebanon Hospital, Los Angeles, California.

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Table 1

Exp't.	Procedure	Total No. of mice	Bleeding Volume (% body wt.)	"P" Value[1]	Hemoglobin Retention in Liver (% normal)	"P" Value
A 1	No burn; no treatment	50	5.42 ± 0.20[2]	<0.01[3]	100	
B	Burn; no treatment	50	2.02 ± 0.14		177 ± 13	
C	Burn; water (5% body wt.) administered by stomach tube	50	2.27 ± 0.16	>0.4[3]	167 ± 16	>0.6[3]
D	Burn; isotonic saline (5% body wt.) administered by stomach tube	50	2.66 ± 0.10	<0.02[3]	137 ± 10	<0.05[3]
A 2	No burn; no treatment	30	5.31 ± 0.09			
E	No burn; water (5% body wt.) administered by stomach tube	30	5.56 ± 0.11	>0.1[4]		
F	No burn; isotonic saline (5% body wt.) administered by stomach tube	30	5.83 ± 0.14	<0.01[4]		

1. In all cases "P" value of less than 0.05 indicates a significant difference of the mean.
2. In all cases the values indicated are mean ± standard error of the mean. Standard error of the mean= $\sqrt{\frac{\Sigma \Delta^2}{n(n-1)}}$
3. Comparison is made with Experiment B.
4. Comparison is made with Experiment A 2.

a continued loss of plasma into the injured extremities. They concluded from this and other data that the quantity and pressure of the extracellular fluid are as important in determining the size of the plasma volume as is the concentration of circulating plasma protein.

Amounts of saline equivalent to 5 per cent of the body weight do not restore the bleeding volume of burned mice to normal levels. Likewise, vascular congestion is not entirely reduced by such amounts of saline. In tourniquet-shocked mice, Tabor and Rosenthal[12] were unable to restore completely the bleeding volume with intravenous injections of saline as high as 10 to 15 per cent of the body weight. Pronounced restoration of bleeding volume occurred after replacement of tourniquets at a time when local swelling of the injured legs was near the maximum. They concluded, as we have,[6, 9] that unknown local factors may play an important role in the circulatory impairment.

The fact that isotonic saline increased the bleeding volume of normal mice, whereas equal volumes of distilled water did not increase the bleeding volume, may have clinical implications in patients with congestive heart failure with increased circulating blood volume. It has long been recognized that the sodium ion is deleterious to patients with heart disease, whereas water is not harmful.[3] In view of the observation in this report, sodium could cause a further increase in blood volume, which would be deleterious to these patients. In addition, Reaser and Burch[10] have found that in congestive heart failure, there appears to be diminished excretion of sodium by the kidneys which would considerably augment the deleterious effect of sodium.

SUMMARY

Orally administered isotonic saline solution in a volume equal to 5 per cent of the body weight increased the bleeding volume of normal mice and prevented to a slight but statistically significant extent the expected reduction in bleeding volume of burned mice. A similar volume of distilled water had no influence on the bleeding volume of either normal or shocked mice.

Isotonic saline solution, but not distilled water, decreased the amount of vascular congestion in the livers of exsanguinated burned mice.

The therapeutic value of sodium after thermal injury is due in part to its action in decreasing vascular congestion with a subsequent increase in bleeding volume.

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The Role of the Psychiatrist in Cardiovascular Disorders

Alexander Simon, M.D., *San Francisco*

THERE is no doubt that physiological changes accompanying emotion may disturb the function of an organ, nor that, through the mediation of the autonomic and endocrine systems, changes in the tension of smooth and striated muscle, in secretion, circulation and respiration may occur. The inevitable conclusion is that there is no logical distinction between mind and body; that we cannot separate the functional from the organic; that it is no longer a question of whether a disease process is either psychologically or organically conditioned, but rather how much is it of one and how much of another.

Remarking on this tendency to an "either/or" concept, Crookshank[4] wrote, "It always seems to me odd in the extreme that doctors who, when students, suffered from frequency of micturition before an examination, or who, when in France, had actual experience of the bowel looseness that occurred before action, should persistently refuse to seek a psychical correlative—not to say an etiological factor—when confronted with a case of functional enuresis or mucous colitis. I often wonder that some hard boiled and orthodox clinician does not describe emotional weeping as a 'new disease,' calling it paroxysmal lachrymation, and suggesting treatment by belladonna, astringent local applications, avoidance of sexual excess, tobacco and alcohol, and a salt free diet with restriction of fluid intake; proceeding, in the event of failure to early removal of the 'tear glands'."

Psychological and somatic phenomena occur in the same biological organism, but we can study and understand the former only by psychological methods and the latter through physics and chemistry. In the presence of a constant or periodically recurring emotional state there are certain physiological concomitants, and it is postulated that chronic disturbances in function tend to be crystallized into structural somatic, perhaps even irreversible, changes.

Certainly most of the patients we see with complaints referable to the heart do not suffer from organic heart disease, and this is not difficult to understand when we realize that anxiety, with its somatic expressions in the cardiovascular system, is a universal phenomenon. Complaints of heart consciousness with or without cardiac arrhythmias, precordial pain, fear of death from a heart attack, respiratory consciousness, and fainting attacks are common symptoms presented to us by patients.

The problems which present themselves to the cardiologist and in which psychological factors may be of particular importance are:

1. The delirious reactions occurring in those patients who show evidence of decompensation.
2. The effect of anxiety on the diseased heart.
3. The problem of neurocirculatory asthenia and its relationship to psychological conflicts.
4. The importance of psychological factors in those patients suffering from cardiac arrhythmias, anginal symptoms and coronary disease.
5. The problem of the relationship of hypertension to emotional tensions.

A. *Cardiac Delirium:*

It is just as important to recognize the early signs and symptoms of a delirious reaction in a patient with heart disease as it is to recognize the early signs and symptoms of decompensation in the circulation; for as the delirium progresses and restlessness and disturbed behavior increase in intensity, this in itself is conducive to further breaks in compensation. One need not wait for the development of bizarre behavior, delusions and hallucinations, since clouding of consciousness and difficulty in mental grasp appear early in the development of such a reaction. Sustained effort and concentration become impaired, and the patient's speech rambling, diffuse and disconnected. Memory is impaired and affective disturbances of doubt, perplexity, anxiety, fear and suspicion may occur. With depression of cerebral metabolism there is a decreased control of emotions and instinctual drives. Urgings, strivings, fears and conflicts poorly repressed in daily life may all be expressed in the delirium. The form and content of this delirious reaction is not specific to the patient with heart disease any more than it is dependent on the nature of any other physical or chemical precipitating agent. It depends, rather, on the personality problems and integration of the individual.

The principal points to emphasize in the treatment of such a reaction are:

1. The avoidance of restraint, since restraint only leads to more struggling and resistiveness with consequent exhaustion.
2. If drugs must be used, morphine in amounts sufficient to allay anxiety and tension is the drug of choice rather than any of the barbiturates which are delirium-producing agents themselves in sensitive individuals.
3. Most delirious patients are frightened. Since they are apt to misinterpret stimuli, it is necessary to reduce these to a minimum; the room should be well lighted and a nurse by the bedside. Familiar faces and surroundings may do more to quiet such a disturbed patient than most sedation we can offer.

From the Langley Porter Clinic and the Division of Psychiatry of the University of California Medical School.

Read at a meeting of the Heart Division of the San Francisco Tuberculosis Association, October 31, 1947, San Francisco.

B. *Effects of Emotional Tension on the Patient With Organic Heart Disease:*

In the patient with organic disease of the heart, it is sometimes very difficult to differentiate what symptoms are inherently a part of the disease process, what are secondary to the heart disease because of necessary restriction in activities, and what symptoms are being unconsciously utilized by the patient as a defense or in order to control the environment. Even if a patient has an organic disease of the cardiovascular system, and perhaps because of it, he may be suffering from psychological conflicts with resulting anxiety and tension which add further burdens to an already poorly functioning heart.[9]

The patient with organic heart disease is apt to exploit his disability; he may deny or minimize the serious character of his illness; he may adopt a martyr-like attitude and attempt to win the respect and admiration of his fellows by displaying how "he can take it," and in so doing neglect the advice of his medical advisers and find himself in repeated decompensation. Often an attack of illness will be precipitated by an intense emotional experience, but more often it is the result of compensatory efforts to attain approval by showing others how ably he can function.

Disturbances in breathing, palpitation and frankly hysterical manifestations may appear even when the heart is well compensated, and cannot be wholly explained by organic disturbance. They can better be understood in terms of frustration as the individual makes attempts to deal with his environment and fails.

The diagnosis of congenital, hypertensive or rheumatic heart disease does not necessarily imply a life of invalidism; and psychotherapeutic efforts must be directed at preventing such a chronic invalid reaction. Care must be taken that the physician does not fall into the trap laid by such a patient's unconscious need to suffer, so that becoming an invalid implies being nursed and cared for. On the other hand, the patient may react to his disability and reduction in activity with feelings of inferiority and inadequacy to which he responds by withdrawal or aggressive hostility; the smouldering repressed anger of withdrawal leading to as severe consequences as the overt anger of the aggressive reaction. Only if the physician recognizes these tendencies in his patient can he help to impart sufficient insight in him to recognize these trends and handle them accordingly. When a patient displays repeated bouts of decompensation while under an apparently adequate regime, the possibility that unconscious compulsive psychological needs have driven him to activities beyond his limitations must be recognized. If a good and strong relationship is built up with the patient, his need for the physician's approval may be sufficient to prevent him from overextending himself. Relief from all responsibility and marked limitation in activity are not always therapeutically wise if the patient's psychological, as well as his physiological, needs are considered.

C. *Neurocirculatory Asthenia:*

Individuals who cannot meet the stress and strain of life situations may develop symptoms related to the cardiovascular system. The normal heart can certainly meet the demands of extreme effort beyond the work required of an individual in his daily activities, but when the individual finds himself unable to perform his assigned duties because of severe symptoms apparently related to myocardial function, one must consider not only the physiological state of the cardiovascular apparatus, but the person himself, his attitudes, feelings, motivations, frustrations and fears.

Neurocirculatory asthenia is such a condition. DaCosta's first description of this syndrome[5] pictured it as the sequella of an exhaustive disease. During World War I it was regarded by many as a definitely "organic disease," and the name of "soldier's heart" was assigned it. Sir Thomas Lewis[7] thought it resembled the picture one sees when the individual is placed under conditions of great effort and the name of "effort syndrome" was assigned. As psychiatrists became interested, it was apparent to them that the resemblance between neurocirculatory asthenia and the anxiety state was remarkable, and they emphasized that the syndrome was a psychogenic one.

The dyspnea of neurocirculatory asthenia is matched by the choking sensations, increased sighing, and feeling that one is not going to be able to take another breath, that is displayed by the individual with repeated acute anxiety attacks. In both conditions the patients may have occipital headaches described as feelings of compression, feelings of tension, and "nervousness," heart consciousness in the form of palpitations, sensations of "butterflies" in the epigastric region, feelings of fear, anxiety and apprehension, marked feelings of fatigability and weakness, tremor and shakiness, precordial distress, feelings of compression about the chest like a "load on the chest," vertigo, fear of or actual fainting spells, anorexia with loss of weight and moods of depression. In only one symptom do the patients whose disease is diagnosed by the cardiologist as neurocirculatory asthenia differ from those whose distress stems from the anxiety states: The patients with neurocirculatory asthenia complain more often that almost any muscular effort will bring on an attack, and this is less often heard from the patients with anxiety states. Almost every one of these symptoms can be produced by hyperventilating the patient. In short, this is probably the same syndrome, although named "neurocirculatory asthenia" by the cardiologist and "anxiety state" by the psychiatrist.[10] There are no specific physical findings or laboratory studies which can help differentiate the two. When there are propounded such a variety of theories of causes as that the disorder is due to prolonged physical strain, infections, overactivity of the thyroid, hyperirritability of the autonomic nervous system, overindulgence in tobacco, hereditary taints, and "psychic instability," it might be better con-

sidered as a disturbance of a total personality in relation to his environment, since whenever the organism is subjected to physical or psychic trauma the heart is apt to be the source of many uncomfortable sensations. Moreover, in evaluating the histories of many of these patients, it is found that they have suffered from similar symptoms of more or less the same character and intensity off and on, more or less, for most of their lives. Exaggerated fears in childhood, frequent nightmares, enuresis often extending into adolescence, are indications of the neurotic-like pattern that many of these patients displayed in their early years, a pattern extending often into adult life when it is expressed in terms of diffuse fear and anxiety especially about physical health.

This leads to shopping from physician to physician with various diagnoses of organic heart disease to "nervous heart," the former being treated with digitalis and rest, the latter with sedation and a slap on the back and "go home and forget it." Most of such patients have been told that they were physically well and yet they continue to suffer from frightening symptoms, and since they receive no relief they become resentful and mistrustful of doctors, their pent-up anger and resentment bursting forth in periodic anxiety panics expressed as a fear of death. In many of them there is a history of poor sexual adjustment and of inadequate discharge for strong feelings of sexual excitement.

Once the defenses of these patients are broken down by some change of emotional import in their immediate environment, severe somatic symptoms are added to their overt neurotic manifestations, and they are apt to retreat into a life of chronic invalidism. Their cardiac symptoms help to rationalize their inner conflicts and fears, and offer them a reason for their sexual inadequacy. They are unconsciously afraid they will lose the approval of those about them, and their illness serves to gain them the attention they fear they may lose.

Therapy of a superficial character and directed along lines of utilizing an authoritarian, Jehovah-like approach, combined with explanation of symptoms and kindly, sympathetic reassurance, apparently result in sufficient improvement that symptomatic recovery occurs in 25 per cent to 30 per cent,[3] but since so many of these patients present phobic symptoms also, sometimes of a severe character, more intense psychotherapy for these is indicated.

D. *Coronary Occlusion and the Anginal Syndrome:*

The patients who suffer from angina and/or coronary occlusions are remarkably similar in personality structure.[6] They are individuals who drive themselves and endeavor to reach the top by hard work and effort. They lay out a plan for themselves and persistently stick to it until they have reached their goal. They show a marked sense of responsibility for their family and dependents, but, in spite of all this, impress one as suffering from an inner sense of loneliness. In constrast to the patients with neurocirculatory asthenia, seldom, if ever, do they display overt neurotic traits, and whatever feelings of frustration or depression they may have, they keep within themselves. They are apt to lead rather narrow, rigid lives, their compulsive drive to work leaving them little time for leisure or hobbies. An exposure to emotional shock, the loss of a loved one, or the necessity to relinquish any hard-earned success, may be the precipitating event before the first attack or the onset may be in the middle of the night following a disturbing dream. Such an onset is often preceded by a long period of overexertion, working long hours, with lack of sleep and overindulgence in tobacco and coffee, and lack of vacation and recreation.

In spite of illness, these people persist in fighting on, and, in order to do so, tend to minimize their symptoms; and if their activities should be severely curtailed, they are apt to react with severe depressive feelings. Even before their illness they harbor thoughts that they may not reach the pinnacle of success they have set for themselves, and if illness overtakes them before they reach their goal, a sense of depression overwhelms them.

In the treatment of such a patient, the first impulse is to correct the unhygienic habits in which he has indulged—the excessive use of coffee and tobacco, the too long hours of work without rest, recreation or vacation, the irregular eating habits and the tendency to work at top speed as if there were insufficient time left for him to accomplish his goals. But advice along such lines is often not enough, and the patient continues to do as he pleases despite the admonitions of his physician. If he does accept his advice, he does so with evident resentment and sometimes severe depression. If the time is taken to explain to the patient what lies behind his compulsive drive to hard work so that he understands himself better, the physician may be rewarded with greater cooperation and gradual decrease in tension. Such patients are generally quite intelligent and quick to appreciate the importance of emotional components in their illness. Another important aspect of therapy is to channel the patient's energies into some outlet which will afford him emotional satisfaction.

E. *Hypertension:*

Patients suffering from hypertension are generally described as displaying a superficial manner of self-control, but occasionally explosive anger and irritability burst through this.[2] They worry over their jobs, everything must be just right, and in this they display their compulsive drive to perfectionism which may be so intense as to interfere in the achievement of their goals. Their tendency to drive themselves with hard work resembles a similar attribute in patients with coronary disease and peptic ulcer. They like their food; eating affords them a sense of satisfaction, helps in relieving their tension and is one of the factors involved in the development of obesity which is so common among them. They dislike and resent criticism. However, they do not overtly express their anger, but tend to repress their feelings. Outwardly they act as though they want to please

people and gain their approval, and inwardly they may be "mad as hell." As a result they are in a psychological turmoil because of the conflict between their need for approval and their need to express the anger which they repress. They want to be well liked, but the occasional bouts of anger which break through their superficial armor often interfere with this. In general, they display few overt neurotic symptoms, although this may not be true of many of the patients that the internist refers to the psychiatrist. In these, the headaches, dizziness, precordial distress, feelings of faintness and fatigue are out of all proportion to the disease, and are manifestations of overt anxiety. A headache may be a symbolic expression of the individual's repressed rage—it is as if he were beating his head against the wall. Fatigue is more often the expression of emotional energy drained off to such a degree because of conflict that there is little left for motor activity. The whole gamut of symptoms displayed by the patient with neurocirculatory asthenia may appear in the hypertensive individual, and this is evidence of his underlying anxiety and indicates that his previous defenses have broken down.

There can be no doubt that psychological factors play a role in the production of hypertension, and we admit this when we allow for the emotional element every time we take a blood pressure reading. When we reassure a hypertensive patient and recommend isolation and rest for him, we do so in the hope of relieving stress and reducing his blood pressure. Not every individual with chronically repressed anger and rage develops hypertension, but at least the psychological factor should be considered as one of a multiplicity of elements which constitute the problem.

These patients need much in the way of reassurance and explanation. Their questions should be patiently heard and answered. In people with pent-up anger and resentment, one should think twice before advising absolute bed rest; some kind of light activity should be considered for them. One cannot rely on sedation alone to solve an individual's problems. The character of such a patient's occupation and his interpersonal relationships on the job may be important. He may be in a position where his hostility is frequently aroused and he has little opportunity to express it. A change of job may be indicated, but it is important that the patient have some appreciation of the fundamental reasons for this.

Where serious organic involvement is present, psychotherapy cannot reverse an irreversible process. Appropriate treatment may not lower the blood pressure in many cases, even in those where organic changes are not yet evident, but it may result in benefit to the patient by the alleviation of many presenting symptoms. In the treatment of such people, one attempts to gradually bring to the surface the sources of their hostility and to interpret this in terms of their present situation. At first they are afraid to give vent to their aggressive impulses, but when the physician is permissive and understanding about them, it helps to relieve their inner tension, and sometimes this reduction is measured on the sphygmomanometer. Our state of knowledge is such that psychotherapy may not be a panacea for the treatment of hypertension, and general medical, drug, and surgical therapy may be indicated, but none of these will relieve a patient of his psychological problems and neurotic conflicts. Not every patient is a suitable subject for psychotherapy—the less overtly neurotic he is, the better his adjustment prior to the development of his illness, the more easily he grasps possible relationships between his somatic difficulties and emotional problems, the better the prognosis with psychotherapy. When the patient tends to deny any and all emotional conflicts, the chances for successful treatment are minimal.

TREATMENT

Many emotional disturbances can be understood and handled if time is taken to learn a little more about an individual as a person, about the setting in which his symptoms occur and about the feelings and attitudes toward the people with whom he works and lives. They require some sensitivity on the part of the physician and appreciation of problems with which people cope. This does not necessarily imply unnecessary and awkward probing into sensitive areas, but the physician need not hesitate to inquire about the source of obvious anxiety. An attitude of kind, sympathetic understanding, devoid of moralistic censure, will assist in making this task easier for the patient.

When the doctor is faced with the problem of chronic invalidism, the therapeutic goal should be an acceptance by the patient of the realities of his disability, but he should be encouraged to utilize to the full his remaining capacities. Faced with a chronic illness, the patient may develop attitudes of depression, resentment, and loss of self-confidence, and these may become exaggerated as he finds his environment unwilling to assume full responsibility for him.[8] An appreciation of such emotional factors may help in a very material way in reducing the number of cardiac invalids so that patients avoid undue cardiac preoccupation and the multitude of neurotic symptoms which follow.

We must recognize that a patient's attitudes toward a doctor vary considerably—from blind child-like acceptance of the doctor as an omniscient God-like figure, to overt hostility and antagonism—and that such attitudes are primarily dependent on previous patterns and experiences in relation to people in authority. If we insist on a stereotyped authoritarian attitude of, "Since I tell you you have no heart disease, you have none," it may be successful with dependent submissive individuals, but it arouses irritation in others who would like an intelligent discussion and explanation of their symptoms and feelings.

We must appreciate and recognize not only the varying attitudes of our patients toward us and deal with them appropriately, but we must be cognizant of our own attitudes to patients. We unconsciously occasionally become hostile to patients, especially if

they "perniciously" persist in not improving under our therapy or deliberately disregard our sage advice.

When a patient presents himself with complaints referable to his heart, a complete and thorough physical examination should be followed by a definite and dogmatic statement in a self-assured manner of physical normality, if that is true. That in itself can be potent psychotherapy. The doctor must avoid expressions, verbal or by attitude, which will raise doubts in the patient's mind, or which will initiate the idea in him that his heart is abnormal.[1] An apparently innocent question or a frown may be enough to incite a storm of anxiety in the patient. The doctor who talks too much and too soon about murmurs and high blood pressure may cause more serious disease than a good many pathogenic organisms. An internist[3] has recently written: "Perhaps the physician should have a personal creed in respect to the handling of patients and particularly apprehensive ones. Such a creed might consist of something like the following.

"First, I shall avoid any thoughtless expression, deed or statement that might initiate in a healthy or relatively healthy patient the idea that the heart is abnormal; briefly, I shall not be a party to iatrogenic heart disease.

"Second, I shall not bring precise instrumental and laboratory methods, such as electrocardiography, into disrepute by consciously gainful or ignorant misinterpretation.

"Third, I shall discourage excessive dependence of any patient on a physician, but I shall give freely of time and try to think of satisfaction of the patient."

Reassurance may be a powerful weapon in combating anxiety, especially if it conveys the competence, honesty and interest of the doctor, but if anxiety persists in spite of reassurance, then a more incisive approach becomes necessary. The reassurance must be based on facts as the physician has learned them. It must consist of more than a slap on the back and a patronizing, "Forget it, don't worry, you'll be all right." That is not psychotherapy, that is "psychosyrupy." The statement, "Forget it, it's all in your imagination," can do more harm than an incorrect diagnosis. Some explanation of the meaning of physical symptoms that arise from states of fear, anxiety and tension, pays dividends. When reassurance fails, one is usually dealing with a more deep-seated neurosis, and if the physician reacts with irritation to his patient's failure to accept his pearls of wisdom, he is only doing so to allay his own sense of failure, and he thereby lessens his therapeutic usefulness to the patient.

The goal of therapy should be a solution of the immediate presenting problem. An effort should be made to assess the patient's assets and liabilities in psychological terms. One cannot remove every stress from the patient. Insight is important if the patient is to adjust, and it is important that insight develop from the patient himself. We must be alert to his implied needs for support and dependence and the expressions of his aggressions and hostilities, how these needs have been satisfied or thwarted, and how he has reacted to such situations. The physician cannot approach such a problem in a cold and ruthless fashion. The patient sets the tempo for the interview. As your examinations and studies are completed, and as the patient's appreciation of your interest in him mounts, his confidence in you increases further, discussion of physical symptoms naturally leads to the emotional and interpersonal setting in which they occurred, and, with an elaboration of this, one learns more of the inner meaning of his symptoms. A discussion of his interpersonal relationships in his own family, with friends, in work and in play, the sources of his irritations, the thwarting of unreached goals and unsatisfied desires, can tell us much about him as a person. One must learn to listen, and it is not necessary to lecture or deliver a sermon. Free emotional catharsis can be a useful procedure, but will only lead up a blind alley if the physician does not recognize the basic emotional needs and drives of the patient. Where insight does not develop, then changes in environment or in the attitudes of people about the patient may be indicated, but do not advise a vacation for your patient solely because you would like to have one yourself.

Above all, "The physician should remember that the illness is a dispute between the patient and his disease and that results will be discouraging unless equal attention is paid to both participants in this dispute."[6] And this involves the cooperative efforts of internist, surgeon and psychiatrist.

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Anesthesia in Thoracic Surgical Operations

L. M. Taylor, M.D., *San Bernardino*

With surgical invasion of the thorax increasing in frequency, anesthesia for thoracic surgery may present its problems at any time to any anesthetist. The conduct of anesthesia for thoracic operations has made remarkable progress since the first successful intrathoracic resection was performed in this country 50 years ago.[14] Development of anesthesia in this field has required a fundamental understanding of the normal and abnormal variations of respiratory and circulatory physiology that occur during major thoracic operations.

The problems of anesthesia for such operations are primarily those of:

1. Providing adequate pulmonary ventilation and gaseous exchange.
2. Providing the surgeon with satisfactory access to the operative area.
3. Control of reflexes affecting the cardio-respiratory system.
4. Maintaining circulatory efficiency.
5. Control of tracheobronchial secretions.

Successful use of the various anesthetic agents is well covered in the literature. Ether has been recommended as the drug of choice.[2,3,17] Cyclopropane appears to be the agent most commonly used in pulmonary resections.[7,9] Nitrous oxide with avertin and ethylene is advocated by some workers. Curare with nitrous oxide, to abolish all spontaneous respiratory efforts, used with controlled respiration appears to offer an improved technique in open chest operations.[10] Spinal anesthesia has its advocates although now it is probably being used less frequently because it renders intubation and tracheobronchial aspiration difficult.[4]

The agent, however, is probably not as important as the manner in which it is administered. Adequate ventilation in the surgical pneumothorax is dependent upon the degree and extent of pulmonary disease, the patency of the tracheobronchial tree, the position of the patient, and the extent of the surgical procedure. When the chest is opened widely, air rushes into the thorax through the opening as the chest wall expands, quickly equalizing the negative pressure created by the chest wall expansion. As the chest wall contracts during expiration and air is forced out of this large opening, very little air is forced out of the lungs through the smaller opening in the trachea. In addition, the mediastinum deviates to the unopened side during inspiration, since the air intake through the chest wall opening is much larger than that through the trachea. Therefore, the lung on the normal side does not expand adequately. The amount of shift of the mediastinum will vary with the position of the patient on the operating table. If the patient is lying in the usual position with the side on which the operation is being done uppermost, the weight of the heart and mediastinum will compress the good lung, requiring the use of more positive pressure to ventilate that lung. When the patient is supine the mediastinum tends to remain in the midline. The improved pulmonary ventilation and minimum spread of bronchial secretions as the result of opening the chest anteriorly may cause surgeons to use this approach more frequently.

Methods to ventilate the lung in the presence of the surgical pneumothorax have included the use of operating rooms in which the air pressure is alternated, endotracheal insufflation, and finally the use of the wide bore endotracheal tube for endotracheal inhalations. Endotracheal intubation is considered by most workers to be essential in this field. Its use assures (if it does not kink) an airway at all times, through which secretions may be aspirated. Moreover, with the use of the inflatable cuff, it provides a gas-tight system allowing the use of positive pressure. Proper gaseous exchange is assured by applying through the trachea a pressure greater than atmospheric pressure. The use of continuous positive pressure has been recommended by some and condemned by others.[2,8] Increased pressure has been shown to cause: (1) rise in venous pressure; (2) decrease in arterial and venous blood flow with lengthening of the circulation time; (3) interference with the elimination of carbon dioxide, and (4) retardation in the entrance of blood into the right side of the heart. Controlled respiration is used routinely by many workers.[12,13] Its advantage is that a smoother and quieter operative field is provided; its disadvantage is the occasional inconvenience to the surgeon caused by the billowing of the expanding lobe or lobes. Increasing the pressure in the airway, whether by the techniques of positive pressure or differential pressure, is used to prevent collapse of the sound lung, to demonstrate lines of demarcation, to stabilize the mediastinum, and to assist expansion of the collapsed lung at the time of closure.

Unfavorable cardiovascular reflexes occur during tracheal and bronchial intubation and have been reported in detail.[16] Investigation has shown electrocardiographic changes consisting of extra systoles, both auricular and ventricular, delayed conduction time, slowing of the heart, and ventricular escape. Reflexes initiated by wide rib spreading and surgical manipulation about the hilum have been described by many workers.[3,11,12] These reflexes, considered initiated by vagus stimulation, consist of irregular respirations, periods of apea, and marked circulatory disturbance, including hypotension and bradycardia. They occur most often at the time of clamping the bronchus. Large doses of atropine,[15] procaine infiltration of the hilar region, and avoidance of light levels of anesthesia are used to obtund this vagal reflex.

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An Army general hospital in the United States to which the author was attached was one to which the patients came for thoracic, orthopedic and general surgical treatment. Anesthetic procedures were performed in accordance with the available personnel—generally one medical anesthetist and nurse anesthetists trained in the hospital. Procedures for thoracic surgical operations were accorded with the desires and requirements of the surgeons. Of 222 thoracic surgical operations performed, 141 were intrathoracic. The patients varied in age from two months to 67 years, the male to female ratio was about 20 to 1. There were no deaths attributable to anesthesia. The intrathoracic operations were for the removal of foreign bodies within the organs of the thorax, removal of tumors and cysts of the lungs and mediastinum, decortication of lungs, drainage of lung abscesses, cardiolysis, pneumonectomies, lobectomies and repair of diaphragmatic hernias.

By directive, only procaine, cocaine, nitrous oxide, pentothal, ether and oxygen were available as anesthetic agents. This restriction was a factor in developing our opinion that ether, as Beecher advocated, is a satisfactory anesthetic agent for thoracic operations. Its use was always preceded by sodium pentothal and nitrous oxide, separately or in combination.

Eighty-one extrapleural operations were performed, mainly for plastic repair of the chest wall and for rib resection. Plastic repair of the chest wall was performed on 56 patients. In practically all of them the defect requiring operation had resulted from combat injuries, and in some there had been previous operative repair. These defects varied in size from a small hernia in one intercostal space to the loss of a portion of several ribs. Rib grafts were used in the repair in most cases. Patients with large defects in which the pleura might be opened during the repair were intubated. Satisfactory anesthesia and operating conditions for these extrapleural operations was accomplished by using sodium pentothal supplemented with nitrous oxide and oxygen. Analgesia was increased by the frequent use of intravenous morphine in 8 mg. or 10 mg. dosage. Procaine infiltration and intercostal block were frequently performed by the surgeon, which lessened the amount of pentothal required in lengthy operations. The addition of ether to the mixture facilitated intubation.

One hundred forty-one intrathoracic operations, 45 of which were lobectomies or pneumonectomies, were performed. Premedication in this group generally consisted of a short-acting barbiturate the night before operation, repeated with atropine sulphate, 0.6 mg., one hour prior to induction. Early in our experience anesthesia was induced with nitrous oxide and oxygen to which ether was gradually added. In the patients having bronchiectasis with suppuration the use of pentothal in doses of about 0.5 gm. facilitated induction, and the drug was used more and more frequently for all inductions. Intubation was performed under direct vision, using a 38 or 40 fr. catheter with an inflatable cuff. The tube was secured in place by a specially constructed bite block containing an adjustable tapered circular wedge.

This combination bite block and tube holder functioned very satisfactorily in the patient having teeth and made the use of adhesive tape unnecessary. The inflatable cuff was filled with sufficient air to seal the trachea against a measured bag pressure of 20 cm. of water. The patient was placed in the lateral position and steadied between two small sand bags secured to the table. An infusion of saline was started in veins in the ankle and in the lower, more outstretched arm, and during the operation whole blood was infused. In the earlier cases in the series, the ankle vein was cut down upon and a blunt cannula sutured in place. Subsequent experience, however, proved that venipuncture with a 15 or 17 gauge needle was superior to the cut down procedure.

When the chest was about to be opened, a slight pressure of about 3 or 4 cm. of water was used. When the pleura was opened, intermittent manual pressure of about 6 to 8 cm. of water was applied during the inspiratory phase and the bag released for expiration. Bag pressure was applied just an instant prior to the patient's inspiratory effort, with the result that although spontaneous respiration occurred, the diaphragm did not contract with its usual force. Rhythmic, assisted inspirations at 6 to 8 cm. of pressure allowed the lung that was not adherent to the chest wall to be partially collapsed, with proper ventilation in the closed lung still maintained. As others have described, the assisted respirations should be continual and constant to provide a quiet operative field.[5] The spontaneous assisted respirations usually maintained satisfactory operating conditions, but at certain times controlled respiration was used to provide a quiet operative field. Pressure necessary to ventilate adequately during controlled respiration occasionally caused too much distention of the lung into the operative field.

For right pneumonectomy, left endobroncheal intubation was performed after the chest was opened, by advancing the endotracheal tube into the left stem bronchus under guidance of the surgeon's hand, and the cuff then was reinflated.

Patients with lung abscess were operated upon under pentothal, nitrous oxide and oxygen, which permitted use of the cautery. An endotracheal tube was used to provide for adequate suction if necessary. By experience with these agents it was found that the endotracheal tube was only tolerated well after adequate cocainization of the larynx and upper trachea. This was best accomplished by the use of cannula instillations prior to induction. There was a definite tendency to resist the tube and attempt its extrusion when cocainization was not thorough and complete.

At the completion of the operation the lung was gradually inflated by increasing pressure to about 15 cm. of water in the average case. Patients in whom decortication had been done generally required a pressure of 20 cm. of water. In these cases, expansion was slow and difficult. Occasionally the occurrence of small fistulae prevented the use of sustained positive

pressure during the closure, and the pneumothorax was obliterated by postoperative suction. In practically all cases a large catheter for subsequent drainage and maintenance of negative intrapleural pressure was inserted in a dependent intercostal space. Negative pressure was applied during the closure to counteract the pneumothorax and the tube clamped after closure of the chest. During the operation, tracheobronchial aspiration was performed with a shortened 16 fr. Levine tube with a finger-tip control for intermittent suction. In patients with suppurative diseases frequent aspirations are necessary prior to removal of the diseased lobe. Complete removal of salivary secretions from the pharnyx was accomplished before extubation.

Postoperative bronchoscopic aspiration was done in all bronchiectatic patients and in most of the others who had undergone long operations. By this procedure, varying amounts of secretions could be drawn from the smaller divisions even after apparently thorough catheter aspiration. (It was of interest to note, at the time of bronchoscopy in the nonsuppurative cases, the general absence of bronchial secretions following anesthesia by ether, whereas salivary secretions would be abundant in the pharynx. This observation raises a question as to whether the irritant properties of ether vapor in the lungs has been overly stressed.) After operation, patients were generally transported to the ward without supplemental oxygen inhalations, and those in whom resection had been done were placed in an oxygen tent. Pharyngeal secretions were aspirated during the immediate recovery period.

Unavoidable loss of blood in the necessarily long operative procedures in highly vascular areas contributed to circulatory depression. The manipulation of highly innervated tissues reflexly caused cardiovascular depression, especially in the lightly anesthetized patient. Circulatory support was maintained by infusions of saline and blood started early in the operation. Whole blood from the blood bank was cross-matched in advance and used as needed, Rh negative patients received only Rh negative blood. An average of 1909 cc. of whole blood and 577 cc. of normal saline was used in the lobectomies and pneumonectomies with an average operating time of 4 hours, 20 minutes. No analeptics were used. In cases of sudden hemorrhage the administration of blood was satisfactorily hastened by introducing pressure in the flask.

An unusual case of pulmonary resection presented itself in an infant two months of age with bilateral pulmonary cysts. Satisfactory anesthesia for pulmonary resection in the infant, as well as in the adult, was considered to be best accomplished by an endotracheal airway with assisted respirations of controllable pressure. Accordingly, a midget-sized apparatus was constructed, using the Ayres T-tube principle and adding a B.L.B. bag at the outlet end of the T-tube. A special T-tube was constructed with an accessary opening on the top of the tube, allowing the easy passage of a ureteral catheter through the endotracheal tube for tracheobronchial aspiration. The anesthetic agent was ether vapor and oxygen delivered to the T-tube, with a connection for measuring bag pressure by a water manometer. An endotracheal tube[6] of the step-down type as described by Cole was constructed of plastic and intravenous rubber tubing, the lower portion being 5.5 mm. in outside diameter and 3.5 cm. long while the upper portion was 8 mm. in outside diameter and 8 cm. long. A screw clamp on the outlet end of the B.L.B. bag controlled the degree of pressure. This apparatus had the disadvantage of allowing some degree of re-breathing. The Mayo Clinic laboratories proved that with adults the CO_2 concentration remains about 1.4 per cent when using the B.L.B. mask at an oxygen flow of 8 liters per minute.[1] In view of this, a flow of 3 liters per minute with an infant was believed to permit very little CO^2 rebreathing. Intubation was performed after open drop ether induction. Anesthesia was maintained by oxygen and ether vapor delivered from the gas machine. Adequate ventilation was provided by having a slight positive pressure in the bag and manually assisting the inspiratory phase of respiration with a pressure of 4 to 5 cm. of water. Circulatory support was maintained by a tibial infusion of equal parts whole blood and saline.

The anesthesia and operation were uneventful with no evidence of impaired ventilation or postoperative edema of the airway. Recovery was uneventful and resection of the pulmonary cyst on the opposite side was performed with a similar result two months later. This apparatus has since been satisfactorily used in patients up to four years of age undergoing thoracic operations.

SUMMARY

1. The abnormal physiology and anesthetic problems created by surgical procedures have been considered.

2. Experiences during the conduct of 222 thoracic surgical procedures in a military hospital have been presented.

3. Maintenance of an adequate airway, prevention of anoxia, replacement of lost blood, and the adherence to sound surgical practice are prime factors in the safety of surgical invasion of the chest, regardless of age of the patient.

3517 Valencia Avenue.

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Preliminary Clinical Investigation of Tetraethylammonium Chloride

With Particular Reference to Disorders of the Circulatory System

Paul A. Shea, M.D., Patricia E. Dunklee, M.D., Malcolm J. Tinney, M.D., and Ward Wilson Woods, M.D., *San Diego*

THIS presentation is a report of a research program undertaken principally to observe the effect of tetraethylammonium chloride, with the trade name Etamon*, on coronary artery disease in humans. The authors also had opportunity to investigate the effects of the drug in a number of other pathological conditions most of which were peripheral vascular in nature. A total of 44 patients received Etamon; all but three were patients in the San Diego County General Hospital.

PHARMACOLOGY

Tetraethylammonium chloride is a quarternary ammonium compound structurally similar to acetylcholine. It is odorless, chemically stable, hygroscopic and readily soluble in water. Work on experimental animals by Acheson and Moe[1, 2] has shown that the chief pharmacological action of the tetraethylammonium ion is the blocking of the transmission of both sympathetic and parasympathetic impulses at autonomic ganglia. These investigators demonstrated that the intravenous administration of vasodepressor doses of the drug caused an increase in blood flow through the femoral artery while injection of the drug into the femoral artery itself caused no change in blood flow; hence, the conclusion was that the vasodilatation was not caused by a direct action on arteriolar smooth muscle. It was shown that vasoconstrictor tone is necessary for the action of the drug, for no further vasodepression is caused by the drug after destruction of the medulla or transection of the spinal cord. If, however, the vascular tone be restored in a spinal animal by electrical stimulation of the cord caudal to the point of transection, tetraethylammonium salts again create a fall in blood pressure. If the blood pressure is maintained by a continuous infusion of epinephrine, tetraethylammonium chloride causes no fall in blood pressure, thus the drug does not prevent the direct effect of epinephrine and the site of action therefore must be assumed to be in the sympathetic ganglia.

These investigators further noted that intravenous administration of the drug prevents the response of the nictitating membrane to preganglionic stimulation but not to postganglionic stimulation. By similar techniques it was observed that the tetraethylammonium ion blocks ganglia in the cardio-accelerator and decelerator effector systems.

METHODS AND MATERIALS

In our investigation we have administered the drug to humans exclusively in the vein, using dosages from 1 cc. to 5 cc. (0.1 gm. to 0.5 gm.) given within 30 to 60 seconds. In one case Etamon was given every four hours for 48 hours but in the majority of cases the drug was administered only once a day. The longest period of therapy was 20 days. A 10 percent solution of the chloride salt was used. An interesting feature is that a maximal effect, although transient, is obtained by the injection of 1 cc. (0.1 gm.). Larger doses only cause a more prolonged action. As the drug is poorly absorbed from the gastrointestinal tract, oral administration produces practically

*The drug used in this investigation was given to us by the Parke-Davis Drug Company through the courtesy of Dr. E. C. Vonder Heide.

no effect in doses of 4 to 6 gm. even in patients who responded well to a parenteral injection. All the effects are the same when Etamon is given intramuscularly. These effects, however, are maintained over a longer period of time. There has been no evidence of impaired renal function as measured by urine volumes and excretory tests as a result of the fall in blood pressure. Acheson and Moe have shown that the drug is almost quantitatively excreted in the urine; nearly all can be recovered in 24 hours.

Methods of evaluating actions of tetraethylammonium chloride after administration included the recording of pulse rate and blood pressure at one-minute intervals following injection. Basal pulse rate and blood pressure were determined prior to the giving of Etamon. The skin temperature changes were recorded by use of the McKesson Dermalor before and after injection. All patients with actual or suspected coronary disease were studied by means of the electrocardiograph before and after administration. The subjective responses of the patient were carefully noted and recorded in all cases; and finally, peripheral vascular changes were further measured by the oscillometer. (These results were not recorded inasmuch as it was felt that the findings added little or nothing to the clinical value of the investigation.)

The clinical material included in this program may be noted in Table 1.

TABLE 1.—*Total Number of Cases—44*

I	Coronary occlusion	7
II	Coronary insufficiency	9
III	Buerger's Disease	4
IV	Arteriosclerotic Arterial Disease	8
	(a) With Occlusion	2
	(b) With Gangrene	2
	(c) With Diabetic Gangrene	2
V	Hypertension	7
VI	Miscellaneous	9
	(a) Causalgia	3
	(b) Bronchial Asthma	2
	(c) Thrombophlebitis	2
	(d) Scleroderma	1
	(e) Reflex Dystrophy	1

RESULTS AND DISCUSSION

The general effect we found following intravenous administration of the drug is recorded in Table 2. Those particular effects most frequently noted were: metallic taste, numbness or coldness of the extremities, a fall in the systolic and diastolic blood pressure and an elevated pulse rate. The most undesirable effect was an occasional postural hypotension persisting for an interval of 20 to 25 minutes after the return of the blood pressure to normal. Another undesirable side-effect was difficulty in voiding, particularly in males, as a result of diminished bladder tone.

The seven patients with coronary occlusion proved by electrocardiogram had as constant complaints the characteristic severe precordial, substernal pain and dyspnea. In every instance these were completely relieved in 60 to 90 seconds after administration of Etamon. One of the accepted theories of the cause

TABLE 2.—*Effects of Intravenous Injections*

1. Metallic Taste in 15-20 seconds
2. Numbness and coldness of extremities in 25-30 seconds
3. Incomplete dilation of pupil
4. Sluggish reaction to light
5. Loss of accommodation
6. Tired, relaxed or weak feeling
7. Ptosis of upper eyelids
8. Prompt fall in systolic and diastolic pressure in majority of patients with high pressures and with some with normal pressures, usually within 30-90 seconds
9. Usually there is an elevation of heart rate to 100-120 beats per minute
10. Sweating stops if present
11. Mouth becomes dry
12. There is usually a rise in skin temperature of the fingers and toes equal to that of the thighs, or about 33 degrees
13. Pressures remain depressed for several minutes, then usually slowly return to original level, the Diastolic pressure being first to return
14. Immediate postural hypotension develops and persists after return of blood pressure lasting. along with dilation of pupils and increased skin temperature, for 15-60 seconds.
15. Cessation of forceful gastrointestinal motility lasts until effect of drug disappears
16. Difficulty in voiding, particularly in males, while under influence of drug

of pain in intermittent claudication is a diminished blood flow leading to an anoxic state which, in turn, causes an accumulation of metabolic end-products around the afferent nerve endings, producing a sensation of pain. This theory, perhaps, applies in the case of coronary thrombosis. It has been frequently noted that occlusion of the popliteal artery results in a blanched, painful extremity, and this same picture occurs when the vessel is ligated. In an extremity with an occluded vessel there is a concomitant spasm of all of the peripheral vessels in the extremity. It is probable, therefore, that similar vasospasm causes the pain of coronary occlusion.

Because Etamon is a vasodilator, we used the drug in the immediate treatment of myocardial infarction and acute episodes of coronary insufficiency to observe if any relief of pain would occur. All of the patients in this group had severe heart disease. Three later died—one the next day, one after eight days, and one 14 days after admission. In no instance did death closely follow the use of Etamon, and since the action of the drug is of such short duration it is unlikely that the medication was in any way connected with the deaths. Postmortem examinations of these patients revealed extensive myocardial infarcts.

The blood pressure range in the patients with heart disease was typically low, varying from 90 to 120 mm. systolic. Five of the patients had a return of pain—one in four hours, one in 18 hours, two in 24 to 30 hours, and one in three days. The type of pain was in no instance as severe or disabling as that in the original episode. Etamon was repeated as needed, with consequent relief of chest discomfort. On admission three of these patients received 15 mgm. of morphine sulfate, which did not relieve the pain. Intravenous Etamon was then given, with almost immediate disappearance of the pain.

Having seen some patients with Buerger's disease benefited by a sympathectomy, and believing that the action of tetraethylammonium chloride was similar to that of a surgical interruption of the autonomic nerve supply, we used the drug in four cases of thrombo-angiitis obliterans. In three the results were good; that is, there was an excellent increase in the distance the patient could walk, plus a loss of the distressing, characteristic, burning, stinging rest pain. One of these patients had an extension of Buerger's disease into the hands (he had had a previous sympathectomy for the disease in his lower extremities) and he experienced complete relief of numbness and pain in his hands following therapy. The one failure was in a man who had had bilateral amputation of the legs for progressive Buerger's disease. He was seeking treatment for a cigarette burn on the left index finger which would not heal. The ulcer did not change under Etamon therapy, but as the patient was having little or no pain and refused to stop smoking, no true evaluation could be made. The patients in this group received 1 to 2 cc. of Etamon every day for from five to 20 days. The shortest observation time after administration of the drug was stopped in these individuals was six weeks, the longest ten weeks, and those benefited at the onset of treatment were still symptom-free. (See Table 3.)

TABLE 3

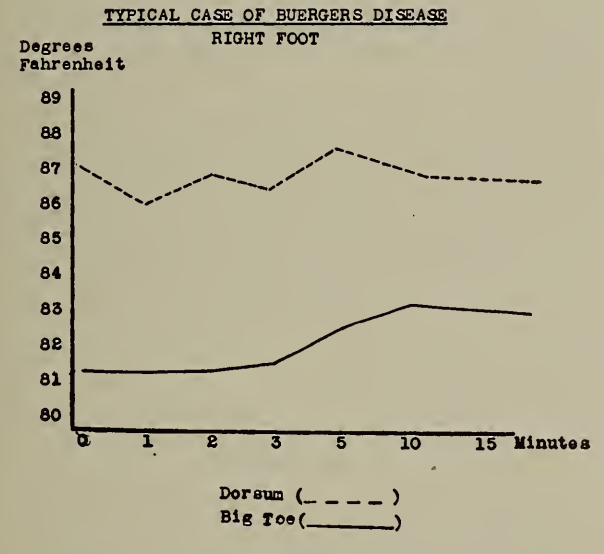
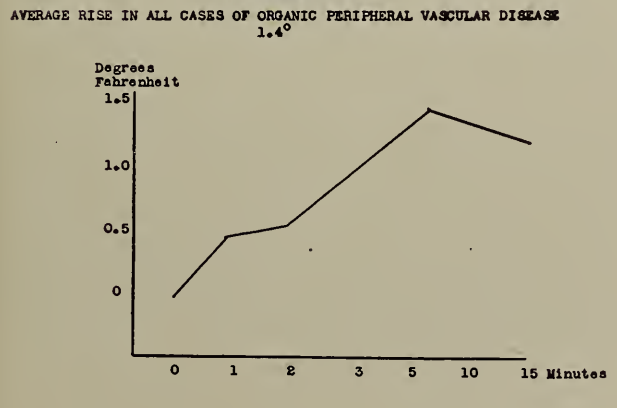


TABLE 4



Etamon was used in treating patients with arteriosclerotic arterial disease which we have divided into three groups: those with occlusion, those with gangrene, and those with diabetic gangrene. Two patients had only intermittent claudication; results obtained in one of them were only fair. Only 1 cc. of the drug was given to this patient, however, and this is not felt to be an adequate trial. Of two patients with occlusion of the popliteal artery, one had moderately good results as evidenced by a rise of 1.8° F. in the skin temperature of the great toe of the affected side and some relief of pain. Results of sympathectomy subsequently performed were about the same, six weeks post-operatively, as the results obtained with the use of Etamon. Patients with gangrene or gangrenous conditions associated with diabetes had no response to the drug and the results were classified as poor. (See Table 4.)

The observation of a rather spectacular drop in blood pressure, especially in the hypertensive individual, following the use of Etamon, suggested preliminary studies of its use as a preoperative test for therapeutic sympathectomy. There were seven cases of hypertension in which the drug was used. The patients in this group were at bed rest for from one to two weeks with the blood pressure recorded twice a day. Etamon in 1 to 5 cc. doses was given intravenously and the results closely observed. The object was to note the degree of blood pressure drop with the drug used preoperatively as compared to the drop obtained postoperatively with a sympathectomy. One of these patients, after administration of Etamon, had only a slight drop in the blood pressure but good relief of symptoms (headache, vertigo, etc.). A subsequent splanchnicectomy has to this date closely approximated the prediction based on the preoperative observations obtained with the use of Etamon. Two patients had excellent drops in blood pressure and relief of symptoms following use of the drug, and these conditions persisted after sympathectomy. However, because of the short intervals of observation following the operations, no great significance can be attached to these observations. Four of the patients had little or no response to the drug and no surgical procedure has been done to date. (See Tables 5 and 6 which present blood pressure studies of all patients receiving Etamon.)

A miscellaneous group of patients who were given the drug included three with causalgia, two with bronchial asthma, two with thrombophlebitis, one with scleroderma, and one with reflex dystrophy. None of the three patients with causalgia had good results, an experience which does not support other sources indicating benefits by its use.[4]

The two patients with severe bronchial asthma had only fair responses—minimal relief of dyspnea. One of these patients has had a subsequent sympathectomy for relief of the asthma and to date has had good relief.

Of the two patients with thrombophlebitis, one had good results as evidenced by disappearance of the redness, swelling and pain two days after the drug

TABLE 5

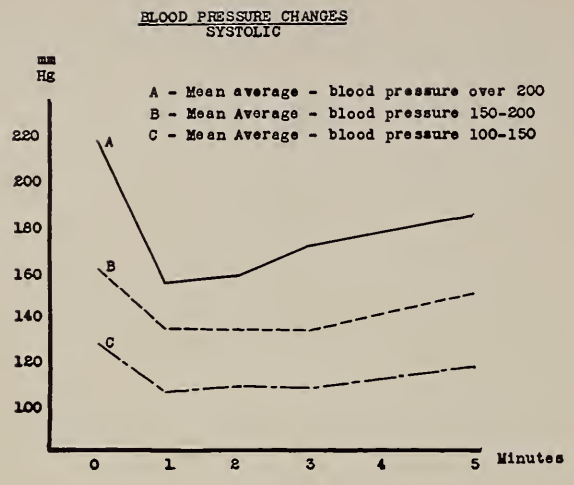
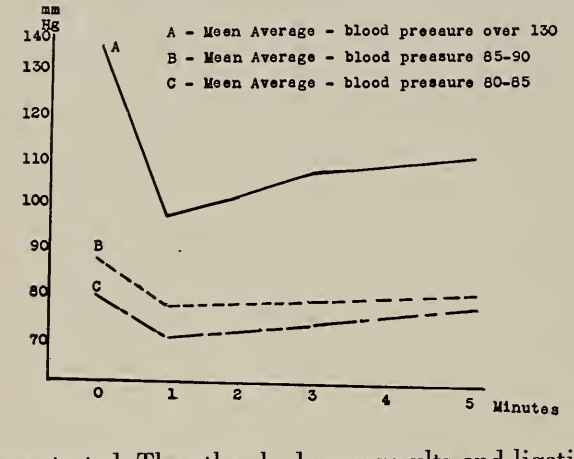


TABLE 6



was started. The other had poor results and ligation was necessary.

The one patient with scleroderma had a moderate response evidenced by a rise of 2.2° F. in skin temperature and tingling of the extremities after administration of Etamon.

The patient with reflex dystrophy had complete temporary relief after the drug was given. A subsequent novocaine block of the superior cervical ganglion produced similar results and a sympathectomy was advised but refused by the patient.

The results of the clinical use of Etamon on the 44 separate patients of this investigation are shown in Table 7. This represents over 400 injections of the drug in doses of from 1 to 5 cc. administered over a varying period of from one to 20 days. We have noticed no toxic reactions during this time and in only one patient was there any untoward effect. This was in a patient with coronary occlusion who lost consciousness for a period of 45 seconds following Etamon administration. The blood pressure in this patient dropped from 184 systolic to 160 systolic, which is not a likely explanation for the response. One of our asthmatic patients had a drop of blood pressure from 220 systolic to 60 systolic but this was only for about one minute and the patient suffered no apparent effect from the drop. Of the total of 44 patients receiving Etamon, 61.2 per cent had satisfactory results (as evaluated by the methods mentioned above) and 38.8 per cent showed little benefit. Fifteen of the 16 patients with coronary occlusion and coronary insufficiency had good results as evidenced principally by immediate relief of chest pain and dyspnea.

TABLE 7.—*Results of Autonomic Blockade with Etamon*

		Cases	Good	Mod.	Fair	Poor
I	Coronary occlusion (Relief of pain and dyspnea	7	7			
II	Coronary insufficiency (Relief of pain)	9	7	1	1	
III	Buerger's Disease	4	3			1
IV	Arteriosclerotic Arterial Disease	8		1		1
	(a) With Occlusion	2		1	1	
	(b) With Gangrene	2			1	1
	(c) With Diabetic Gangrene	2				2
V	Hypertension (All results temporary—5 Min. to 3 Hrs.)	7				
	(a) Blood pressure drop alone					
	(b) Relief of symptoms alone		1			
	(c) Both		2		2	2
VI	Miscellaneous	9				
	(a) Causalgia	3		1	1	1
	(b) Bronchial Asthma	2			2	
	(c) Thrombophlebitis	2	1		1	
	(d) Scleroderma	1		1		
	(e) Reflex dystrophy	1	1			
Total Cases		44	22	5	9	8
Per Cent Results		100	50.0	11.2	19.8	19.0

SUMMARY

1. The tetraethylammonium ion (Etamon) is nontoxic in doses up to 5 cc. daily. The total number of consecutive days the drug may be administered without toxic effects is yet to be determined.

2. The substance apparently blocks both sympathetic and parasympathetic transmission at the ganglia.

3. The pain of coronary artery disease is definitely relieved by the drug.

4. The symptoms of Buerger's disease seem to be ameliorated, at least temporarily, by the use of this drug.

5. Etamon appears to be of little value in advanced arteriosclerotic diseases.

6. As a diagnostic procedure before sympathectomy for hypertension the use of the drug may have value.

San Diego County General Hospital, North Front and Dickinson Streets.

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Q Fever in Central and Northern California

Edwin H. Lennette, M.D., and Gordon Meiklejohn, M.D., *Berkeley*

In a preceding paper,[4] a short chronological history of Q fever was presented, together with a brief summation of some of the epidemiologic findings, especially those made in Southern California[2] by the Q Fever Laboratory at Hondo.[4] Emphasis was placed on Southern California because at the time of writing all the cases of Q fever uncovered were from the area south of the Tehachapi Range. Since the preparation of that report, evidence has been obtained which indicates that more than 100 cases of Q fever have occurred in Central and Northern California.

The purpose of this preliminary communication is to bring to the attention of the physician the fact that Q fever is much more widely distributed in California than was previously thought. Serological data establishing this fact are presented, and the clinical picture of this disease as seen in the Central and Northern portions of the state is briefly summarized.

EVIDENCE FOR THE PRESENCE OF Q FEVER

A serologic diagnosis of Q fever was made when, in the simultaneous testing of paired sera, collected during the acute and convalescent phases of the illness, the appearance, or rise in titer, of complement-fixing antibodies to *Coxiella burneti* was demonstrated. In the absence of serum taken in the acute phase, the demonstration of a high titer of antibody in the convalescent serum of an individual with a recent febrile illness was considered to be strong evidence of infection with this agent.

Representative results of complement-fixation tests with the paired sera of several Q fever patients are shown in Table 1. The maximum increase in titer observed was 512-fold or more (patient No. 8 in the table), the lowest, 8-fold (patient No. 6). A point of some interest, and of considerable importance in the laboratory findings in the diagnosis of this disease, is that the humoral antibody does not appear as early in this disease as in a number of others; e.g., patient No. 4, after 21 days of illness, had a titer of less than 1:8. In this case, neglecting to take a blood specimen very late in convalescence would have resulted in failure to establish a diagnosis of Q fever. We have observed in a number of cases that antibodies may first appear as late as two to three weeks after onset of the illness. For this reason it is advisable that in those instances in which the serologic tests remain negative during this interval, despite the clinical impression that the patient has Q fever, an additional blood specimen or specimens be sent to the laboratory.

Table 2 gives the results of complement-fixation tests on a number of individuals representative of a group who had had an acute febrile illness, the cause of which was undetermined despite intensive laboratory study. Their sera were sent to this laboratory for inclusion in the Q fever survey after the requested serologic examinations had been done elsewhere. The original clinical impressions had been brucellosis, tularemia or enteric fever. Patient No. 1 is included to show that Q fever presumably was present in Northern California at least as far back as January, 1947.

Table 1.—*Representative Results of Complement-Fixation Tests with Sera of Q Fever Patients, Showing the Appearance, or Rise in Titer, of Antibodies During the Course of Illness.*

No.	Patient	County	Onset of Illness	Date Bled	Q Fever Complement Fixing Titer*
1	J.C.	Alameda	4-19-48	4-26-48	8
				5-10-48	256
2	T.B.	Plumas	?	3- 9-48	<8
				4-17-48	1024
3	P.L.	San Joaquin	3-20-48	3-29-48	<8
				4- 8-48	1024
4	L.P., Sr.	Solano	3- 7-48	3-28-48	<8
				5- 6-48	64
5	V.D.	Solano	3-15-48	4- 3-48	16
				4-19-48	512
6	S.K.	Solano	4-13-48	5- 1-48	16
				5-15-48	128
7	L.P., Jr.	Solano	4-23-48	4-23-48	<8
				5- 6-48	512
8	A.D.	Yolo	4- 3-48	4-12-48	<8
				4-26-48	4096
9	S.A.	Yolo	4-27-48	4-29-48	<8
				5-21-48	32
10	L.L.	Yolo	5- 1-48	5- 6-48	<8
				5-17-48	1024

*Expressed as dilution giving +++ or better fixation. Antigen: Henzerling strain of *Coxiella burneti.*

Table 2.—*Results of Q Fever Complement-Fixation Tests with Convalescent Sera of Individuals with an Acute Febrile Illness.*

No.	Name	County	Onset of Illness	Date Bled	Q Fever C.F. Titer*
1	R.G.	Glenn	Jan. 1947†	3-13-48	128
2	J.P.	Sacramento	4-10-48	4-19-48	256
3	B.E.	San Francisco	3- 6-48	4-12-48	1024
4	L.W.	San Joaquin	4-14-48	4-28-48	256
5	T.W.	Solano	4- 3-48	4-23-48	512
6	E.McD.	Stanislaus	1-26-48	3-18-48	1024
7	L.L.	Tehama	4-11-48	5-10-48	256
8	L.O.	Yolo	4-25-48	5-10-48	256

*Titer expressed as highest serum dilution giving +++ or better fixation; Henzerling strain antigen used.

†This person had pneumonitis of undetermined cause in 1947; a blood specimen was taken in March 1948 to determine if the causal agent might have been *Coxiella burneti.*

From the Viral and Rickettsial Disease Laboratory, California State Department of Public Health, Berkeley.

GEOGRAPHIC DISTRIBUTION OF Q FEVER

Results of complement-fixation tests on the sera of approximately 1,000 individuals up to June 8, 1948, indicate that more than 100 cases of Q fever have occurred in California.

The cases have been encountered in largest number in Solano and Yolo counties, but one or more cases have been found in each of 12 other counties. The counties and the number of cases are as follows: Alameda, 1; Colusa, 2; Fresno, 1; Glenn, 1; Monterey, 1; Placer, 1; Plumas, 1; Sacramento, 1; San Francisco, 1; San Joaquin, 2; Solano, 20; Stanislaus, 2; Tehama, 2; Yolo, 70.

CLINICAL PICTURE

The onset of the disease has in most instances been sudden. The presenting complaints have been feverishness, headache, aching in the neck and back, and chills. The latter have been true shaking chills* lasting from several minutes to more than an hour. In some patients rigors have occurred once or more daily for several days. The temperature curve has usually been spiking in character, with peaks as high as 104°-105° F. Respiratory symptoms have been uncommon. Physical examination in the early stages has failed to disclose signs of upper or lower respiratory tract infection or of splenic or hepatic enlargement. Leukocyte counts at this time have been within the normal range, or slightly lower.

The disease has shown marked variation in severity. The majority of patients have recovered promptly following a febrile course of from four to eight days' duration; this has been true primarily in the age group under 30 years. Others, however, and especially those in the older age groups, have run a prolonged febrile course, sometimes lasting a month or more. Pneumonia has not been detected by physical or roentgen examination except in a few instances. Hepatic enlargement and tenderness have been not uncommon in the severely ill patients. Splenic enlargement has been noted as the disease progresses. Thrombophlebitis has complicated the convalescence in three patients. No deaths have been observed in this series.

DIFFERENTIAL DIAGNOSIS

In the initial phases of the illness, the diagnosis most frequently entertained is influenza. This diagnosis becomes untenable as the fever continues beyond five or six days, and particularly if the patient has repeated shaking chills. Consideration is then given to other diseases such as malaria, brucellosis, typhoid and paratyphoid fevers, and tularemia. Brucellosis is suggested by the fact that many patients have a background of contact with livestock.

In patients with pneumonia the symptoms may simulate those of primary atypical pneumonia, psittacosis, tuberculosis, or coccidioidomycosis.

*True rigor has been reported as not observed[1] or uncommon except in severe cases.[5] Frank rigor, however, has been encountered frequently in the cases we have observed or investigated.

The protracted febrile course together with an enlarged, tender liver may lead to a diagnosis of hepatic disease.

LABORATORY AIDS IN DIAGNOSIS

A definitive diagnosis of Q fever can be made only with assistance from the laboratory. A diagnosis can often be made by isolation of the rickettsia from the blood in the early stages of the illness. This involves inoculation of blood into a guinea pig, recovery of the organism from this animal and its subsequent identification. This procedure, aside from the fact that a rather thorough knowledge of the methods used is required, is not recommended under the usual laboratory conditions because of the highly potential danger of infection to personnel working without special safeguards.

Sterile whole blood for serologic examination should be obtained early in the course of the illness and sent to the laboratory. A second specimen of blood should be taken 10 to 14 days after the first and submitted for examination. Both sera are tested simultaneously in the complement-fixation test. Demonstration of the appearance, or of a rise in titer, of antibody is considered diagnostic of Q fever. *A negative result, however, does not necessarily rule out Q fever, as antibodies may appear late, and additional tests therefore should be made with blood taken later in the course of the disease.* We cannot emphasize too strongly both this fact and the fact that two blood specimens, with an appropriate time interval between collection of the two, are required for the diagnosis not only of Q fever, but of other rickettsial or viral diseases as well. Results with a single acute-phase serum specimen have no diagnostic significance and those with paired specimens may be difficult or impossible to interpret if one specimen is drawn too late in the acute stage of the disease or the other too early in convalescence.

Blood drawn during the early course of an illness suspected to be Q fever should be handled with due regard to the possibility that it may contain the rickettsiae and therefore be highly infectious.

CHEMOTHERAPY

Penicillin and sulfonamides have been given extensive trial and have not shown any obvious effect on the course of the disease. Streptomycin, despite evidence[3] that it reduces the lethality of the disease experimentally induced in guinea pigs, has given equivocal results to date.

A new antibiotic (Aureomycin hydrochloride) recently released for investigational use, is currently being tested on patients in California, and offers considerable promise.

DISCUSSION

During the beginning phases of the present survey, relatively small numbers of sera with significant titers of antibody were encountered. Soon afterward (March, 1948), certain physicians, notably Dr. H. M. Thelen of Vacaville (Solano County) and Drs. O. C. Railsback and A. M. Clark of Woodland (Yolo

County), noting the occurrence of an unusual type of acute febrile disease, submitted paired blood specimens with requests that they be tested for Q fever antibodies; it was soon established that numerous cases of Q fever were occurring in the Vacaville and Woodland areas.

Information supplied by Dr. Railsback led to an investigation of an epidemic of an acute febrile disease occurring in another Yolo County community. The outbreak was soon found to be one of Q fever. At least 70 cases have occurred there since February, 1948, the total number being unknown, as the study is still in progress. Evidence has also been obtained that a small outbreak of Q fever occurred in Tehama County during April and May, 1948.

The fact that more than 100 known cases of Q fever occurred in Central and Northern California during the four months, February through May, indicates that the disease is more common than had been believed, and should now be considered in the differential diagnosis of acute febrile illnesses and of the pneumonias of the viral type, especially when there is a history of close contact with livestock. On the other hand, the disease has attacked persons with no such history of close contact (a grocery clerk, a gasoline filling-station attendant, etc.). The method of transmission of the disease has yet to be ascertained. In Southern California, evidence has been adduced incriminating ingestion of infected milk,[2] but were this the main, or sole, means of transmittal in Central and Northern California, one would expect to find frank, clinical cases in women as well as men. This has not been our experience—Q fever in the female appears to be unusual; there are only two proved cases in the present series. That an occupational factor is the basis for this difference in incidence seems probable. Thus, most of the cases encountered in Northern California have been in individuals occupationally in close contact with sheep or goats. Serologic examination of these animals on ranches where the disease occurred in humans has shown a high percentage to possess complement-fixing antibodies to *Coxiella burneti*. In this connection, it might be remarked that unlike the situation in Southern California, where dairy cattle are involved, the number of serologically positive cattle in the north has been very low, so that from present evidence the epidemiologic factors of the disease in the two regions of the state appear to be quite different.

There is every reason to believe that as physicians become alerted to its possible presence, Q fever will be found in areas besides those in Southern and Northern California from which cases have already been recorded.

SUMMARY AND CONCLUSIONS

1. Q fever has now been found in Central and Northern California.

2. From February through May, 1948, more than 100 cases of this disease were found in 14 counties north of the Tehachapi Range. More than one-half the cases have come from one area in Yolo County.

3. Q fever should no longer be regarded as an exotic disease, but should be considered in the differential diagnosis of any acute febrile illness for which the cause is obscure.

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A Fatal Case of Q Fever in Southern California

Don C. Brown, M.D., *Compton*, Leon A. Knight, M.D., *Downey*,
William L. Jellison, Ph.D., *Hamilton, Montana*

ONLY three fatal cases of Q fever have been reported in the United States since it was first recognized by Dyer[3] as a disease of man in this country.

One of these cases occurred at the National Institute of Health when a laboratory outbreak of 16 cases was experienced in 1940. The autopsy findings and histopathologic study of the case were reported by Lillie, Perrin, and Armstrong.[6] The brief clinical record which these authors gave corresponds very closely to that in the case here reported and is quoted as follows:

"The patient was a white male, aged 59, gardener and incinerator operator. Onset as 'cold' on April 17, 1940. Admitted to hospital on April 22, died on April 25. Had slight productive cough and chest pain on inspiration. Temperature on hospital admission 102° F., 103.5° F. maximum. Dullness over right lung from scapula to base posteriorly, smaller area on left.

"X-ray: 'Pneumonitis' of right lower lobe, less on left.

"Blood: 6,200 white corpuscles, 82 per cent neutrophils and 18 per cent lymphocytes."

Two brothers died in an outbreak of the disease in a packing plant at Amarillo, Texas, in 1945. One of these patients exhibited definite evidence of pneumonia. Autopsies were not performed. Diagnoses of Q fever in these cases were based on the evidence that both patients were part of a group of workers involved in an acute epidemic (55 cases) and the epidemic was confirmed as being Q fever by the finding of strains of *Coxiella burneti* (Derrick) in blood specimens drawn from some of the acutely ill patients[1] and by positive reactions in tests on the blood of convalescent patients.[5]

An account of a single fatal case of Q fever in Australia is given in the annual report of the Director General of Health and Medical Services for the year 1936-1937, but this case was complicated by chronic tuberculosis which, no doubt, contributed to the death of the individual. No other fatal cases appear to be recorded in the Q fever reports from that continent and it is quite evident from the reports that severe cases of the disease are seldom experienced there.

Although many cases of Q fever were reported among American troops in the Mediterranean area and in troops recently returned or returning from that area,[4, 7] no fatalities were observed.

While it has been established that the clinical entity known as "Balkan grippe" is in some cases Q fever, there is no warranty for attempting to relate observations on that disease to Q fever without further confirmation. It is of interest, however, to quote from a publication on this disease by Dennig[2] which states, "The prognosis is very favorable; the death rate for example, in more than 1,000 patients that I saw in 1941, was under 1 per cent." This death rate is not inconsistent with that so far observed in Q fever in the United States.

The report of a fatal case of Q fever in a vigorous man is of exceptional interest. The patient became infected in the Southern California endemic area, where the disease was first recognized by Young.[8] The report of the case is complete with a clinical history, findings in routine laboratory studies, x-ray record, autopsy disclosures and protocols of experimental animals in which a strain of *Coxiella burneti* (Derrick) was established.

CASE REPORT

A 43-year-old Caucasian male, employed at the stockyards in Los Angeles County, California, died December 11, 1947, following an acute illness, diagnosed as influenza, which terminated in pneumonia. Diagnosis of Q fever was established by the presence of the infecting organism in experimental animals inoculated with blood drawn postmortem from the body of the patient.

Clinical findings: The patient worked at his regular duties handling cattle at the stockyards on December 2, 1947, although he had been ill for five to eight days with what he considered to be an ordinary head cold. He stayed home and in bed because of illness on December 3. On December 4, when the temperature was noted to be 103° F., a physician was called. One of the authors (D.B.) first saw the patient on December 4. At that time the temperature was 103° and was reported to have been as high as 105°. The patient complained of frontal headache, malaise, and profuse perspiration. There was a slightly productive cough but percussion and ausculation of the chest did not reveal any obvious lung involvement. The patient had been taking plain empirin compound which partially relieved the headache. He was given 200,000 units of penicillin in oil and wax. One gram of sulfadiazine every four hours and other symptomatic measures were prescribed. The patient remained at home and was told he had epidemic influenza. (Influenza "A" was epidemic in the Los Angeles area throughout the months of November and December, 1947.)

When visited again two days later, the patient was mentally confused and remained so for the duration of the illness. He was coughing frequently and perspiring profusely. The left lower lung area was dull to percussion and showed impaired resonance. Hospitalization was recommended but rejected.

There was no marked change in the patient's condition in the next three days. An x-ray film of the chest taken on December 7 with a portable machine was interpreted as showing "an extensive area of increased density from the base to the second rib on the left side. The extreme upper chest and costophrenic sulcus remain aerated to some degree. The right chest is clear." On December 10, the patient appeared to be slightly cyanotic and oxygen was administered at home. The pulse was 120 to 130 and temperatures were spiking to 105°.

A second roentgenogram of the chest taken in the late afternoon was interpreted as showing "the entire left hemi-

thorax to be homogeneously dense, with evidence of a streaky, patchy, consolidation in the right mid-lung extending from the hilum to the periphery. Findings are consistent with pneumonia of the left chest with rapidly progressive increasing effusion with extension of pneumonitis into the right chest. This could well be viral in type." A few minutes after the exposure, while the film was being developed, the patient experienced a convulsive seizure, with difficulty in breathing, and died.

Laboratory Findings: Routine laboratory studies performed late in the course of illness were not especially informative. Results of urinalysis were reported as follows: color, amber; specific gravity, 1.020; reaction, acid; albumin, 2 plus; sugar, 0; pus cells, 1 to 3 per highpower field; epithelial cells, 1 to 3 per highpower field; granular casts, 1 to 2 per highpower field.

On December 8, blood findings were recorded as follows: hemoglobin was 93 per cent; erythocytes numbered 5,000,000 and leukocytes 5,000 with a differential count of 74 per cent polymorphonuclear leukocytes, 25 per cent lymphocytes, and 1 per cent eosinophils.

SUMMARY OF CLINICAL FINDINGS

The conspicuous findings observed during the patient's illness may be summarized as follows: chills, fever, profuse perspiration, weight loss, frontal headache, mental confusion, nasal congestion and mucoid discharge. There was some aching of the back but it was not a chief complaint. The appetite was poor but there was no indigestion, diarrhea or vomiting. At no time during the illness was cutaneous eruption or jaundice in evidence.

The patient had experienced an appendectomy and a herniorraphy about twelve and ten years previously and had convalesced without complications. He did not use drugs of any sort regularly, and he used alcohol and tobacco (cigarettes) moderately. He had been working overtime for the past few months and had lost considerable sleep. Six feet in height, well-developed and well-nourished, the patient had weighed 190 pounds before becoming ill. There was no known history of disease that would have complicated the present illness.

No diagnosis other than influenza with pulmonary involvement had been made at the time of the patient's death. Q fever was not suspected, as the majority of the medical profession in Los Angeles County was not then familiar with the clinical symptoms of this disease.

AUTOPSY

Autopsy was performed about 40 hours after embalming. Previously, three hours after the body was embalmed, 20 cc. of blood was removed from the left femoral vein for study.

During the embalming operation, poor drainage had been observed and many thrombi, 6 to 8 inches long, had been flushed from the venous system.

The pleural cavity contained several hundred cc. of serous fluid. The pericardium contained an excess of fluid. No sclerosis of coronary arteries was noted.

The lungs presented a somewhat dark edematous mottled appearance with generalized anthracosis. The lung tissue was extremely heavy and consolidated, with the exception of a small area in the right upper lobe that seemed fairly well aerated. This was the only area of lung tissue that appeared to be functioning at the time of death. A roentgenogram, taken immediately before death, showed a large central area in the right lung that was not consolidated. On gross sectioning, the lung tissue was found to be firm and filled with watery fluid. No purulent areas were found. Small whitish areas about 2 mm. in diameter resembling areas of necrosis were evident on the surface and deep in the lung tissue. The larger blood vessels of the lungs were opened at the hilum and a fibrinous clot of almost cartilaginous firmness about 7 to 8 cm. long was found in the artery of the left upper lobe. This did not appear to be of post-mortem formation. The hilar lymph nodes showed no enlargement.

The spleen was not enlarged but was extremely friable. When the capsule was cut through, it presented an appearance resembling that found in acute toxemia. The tissue was soft and oozed out of the cut surface. The organ was dark burgundy in color. The liver appeared normal in size and color.

There were mottled patches on the surface of the kidneys, and an area of hyperemia was noted in the right kidney when sectioned. The capsules were easily removed. No other gross changes were observed in the organs of the thorax or abdomen. The central nervous system was not exposed.

The cause of death was considered to be: (1) Atypical pneumonia; (2) Pulmonary embolism secondary to thrombophlebitis of the femoral veins.

HISTOPATHOLOGIC STUDIES

The tissue specimens for histopathologic study were sent to the Division of Pathology, National Institute of Health, Bethseda, Maryland. A detailed report is being prepared by Dr. Perrin and his associates. For the purpose of this report, we quote his summary comment: "The broncho-pneumonia is consistent in type with that seen in a case of Q fever in this laboratory (National Institute of Health). In some respects, it is not dissimilar to the pneumonia seen in psittacosis and other virus infections."

TESTS ON POST-MORTEM TISSUES

Blood: A portion of the sample removed from the femoral vein was injected into guinea pigs within 30 minutes and the remainder was centrifuged. Serum was saved for complement fixation test and the sedimented cells were resuspended and injected into another guinea pig.

This serum sample was tested with negative results at three separate laboratories which had been testing numerous samples for Q fever by complement fixation tests. (Complement-fixing antibodies are not to be expected early in the acute stage of Q fever infection.)

Sternal tissue: A portion of the sternum was saved for animal injection. This piece, containing much red

marrow and blood, was crushed in a mortar with sterile saline, and a heavy suspension was obtained and was injected into four guinea pigs.

One guinea pig injected with blood showed two days of fever of 40.3° C. and 41.0° C., respectively, and was sacrificed on the 12th day; at autopsy the cutaneous edema and induration characteristic of Q fever in the guinea pig were present. The spleen was enlarged and when spleen tissue was passed to two fresh guinea pigs, infection was produced in them. These two guinea pigs exhibited definite scrotal swelling and reddening which is not common in animals inoculated with *C. burneti.* An abundance of rickettsiae was observed in smears of the subcutaneous exudate.

The other guinea pig injected with blood exhibited a fever of 41° C. on the 13th day and 40° C. on the 14th day after injection. A blood sample taken on the 24th day was positive for Q fever by the complement fixation test at a dilution of 1:64 or greater. The guinea pig injected with resuspended blood cells exhibited a febrile course from the eighth to thirteenth day—40.4° C., 39.9° C., 40.6° C., 40.3° C., and 39.9° C., respectively. A blood sample taken on the 24th day was positive for Q fever in a dilution of 1:64 or greater.

All four animals injected with bone-marrow suspension exhibited only low febrile courses, but on the 24th day results of the complement fixation test of the blood of each were positive for Q fever at dilutions of 1:64 or greater. Rickettsiae were observed in smears of exudate aspirated from the cutaneous lesion of one of these animals.

These experimental guinea pigs had been kept in cans in a small laboratory room where other guinea pigs infected with Q fever were present. Control animals were not kept in the same cans but 32 control guinea pigs were kept in the same animal room concurrently with these tests. All were bled and tested for antibodies after 30 days and the tests were negative for Q fever in all the 32 controls.

Tissues from an experimental animal in this series were sent to the Rocky Mountain Laboratory at Hamilton, Montana, and to the National Institute of Health laboratory at Bethesda, Maryland, and both reported the successful establishment of strains of *C. burneti* (Derrick) in guinea pigs by injection of these tissues. (The complement fixation tests reported herein were also made at these laboratories.)

SUMMARY

The first confirmed fatal case of Q fever in Los Angeles County is reported. The patient's occupation brought him in frequent contact with livestock (a characteristic of about 72 per cent of the cases so far studied in Southern California). The clinical course was typical of the disease. The patient was the first under 50 years of age known to have died of Q fever. The clinical history and the gross and microscopic pathological findings were consistent with those of a previous fatal case in America. The diagnosis was confirmed by the isolation of *C. burneti* in experimental animals injected with blood and sternal marrow collected at postmortem examination.

Q Fever Laboratory, Box 685, Hondo, California.

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Another death possibly due to Q fever: A patient who may have had Q fever died at the Los Angeles General Hospital in June, 1947. A blood sample taken late in the course of illness was sent to the National Institute of Health and the result of complement fixation test was positive for Q fever at a titer of 1:128 or greater.

When a report on this test was received at the Q fever laboratory, it was learned upon inquiry that the patient had died. An autopsy had been performed and a diagnosis of Hodgkin's disease made by the pathologist. The antibodies for Q fever may have been evidence of a previous illness. However, a review of the case suggests the patient was ill with Q fever at the time of death, and the high titer observed suggests recent infection with that disease.

Boxer's Bursitis

A. Waxman, M.D., and H. Geshelm, M.D., *Los Angeles*

AMONG 523 injuries to professional and amateur boxers and wrestlers treated in a five-year period, 22 were injuries to knuckles of 21 boxers, all in their early twenties. Twelve of the knuckle injuries, nine in Caucasians and three in Negroes, were diagnosed as simple contusions and complete recovery followed a few days of treatment with hot soaks. In the other ten cases, which form the basis of this report, the diagnosis was occupational or traumatic bursitis involving the metacarpo-phalangeal joints. There were nine patients (one was injured twice) with this diagnosis. All were professional boxers, and a striking feature is that all in this group were Negroes.

Few cases of bursitis involving the hand have been reported in the literature. Cooper[2] in 1942 reported eight cases of calcareous deposits in the metacarpo-phalangeal regions, possible due to trauma; onset was acute in all cases with no history of acute injury or illness. No mention was made of fluid. Rycroft[10] in 1928 reported occupational bursitis of the hand in a railroad carriage cleaner. The disease was in the dorsal medial aspect of the right major thumb opposite the metacarpo-phalangeal joint and was thought to have been caused by constant pressure of the handle of a cleaning brush on the most prominent bony joint. Hayden[4] in 1923 reported a case of traumatic bursitis of the right palmar bursa, along the entire length of the fifth metacarpal bone, in a man who had caught his hand between a heavy rod and the hub of a drive wheel. Howard[5] in 1939 reported a series of 27 cases of subcutaneous dorsal digital bursitis. These were found in relatively young people (average age 30.1 years); more often in men (25 cases) than in women (three cases). They were found in butchers, fishermen and warehousemen, housewives and stenographers. The most frequent site in this series was the metacarpo-phalangeal bursae (13 cases). Of the 27 cases, 12 involved the middle finger and one the thumb. Howard, quoting Spalteholz,[12] describes small bursae lying between the skin and extensor tendons on the dorsum of the finger joints as follows:

1. Dorsal Digital Subcutaneous Bursae—immediately beneath the skin on the dorsal surface of the digital articulations; these are fairly constant over the proximal interphalangeal joint and occasionally over the distal phalangeal joint.

2. Dorsal Metacarpo-phalangeal Bursae. Occasionally occur on the dorsal surface of the metacarpo-phalangeal articulations.

3. Inter-metacarpo-phalangeal Bursae—of frequent occurrence, from one to three in number, small and lying between two neighboring fingers at the metacarpal heads dorsal to the transverse capitular ligaments, between the second and fifth fingers. (Toldt,[13] in his Atlas of Human Anatomy, illustrated these bursae very clearly.)

In our series of ten cases the diagnosis of bursitis was confirmed in each instance by aspiration of bloody or gelatinous fluid from the affected knuckle. Roentgenograms taken in each case showed no damage to bones. In seven cases the treatment was conservative—aspiration of the bursa, hot soaks, adhesive strapping of the joints and physical therapy usually for a period of less than two weeks—and clinical cures resulted. In the remaining three cases (two patients), the bursal sac was excised, with resulting clinical cure.

Four of the seven patients treated conservatively had residual thickening of the soft tissues above the joint at the time they were considered cured. Follow-up observation after an interval of several months or longer, which was possible in six of the seven cases, disclosed no complaints or disease referable to the knuckle that had been treated.

More detailed reports of the three cases in which the bursa was excised follow:

CASE REPORTS

Case 1.—A 22-year-old boxer injured the middle knuckle, right hand, on April 4, 1945. There was swelling and tenderness over the knuckle. On several occasions fluid was aspirated from the bursa. Conservative treatment brought no beneficial results. The sac was excised on April 24, 1945, and the patient was discharged on June 19, 1945, clinically cured. There has been no further trouble referable to this knuckle.

Case 2.—The patient, a Negro pugilist, aged 23, injured the left middle knuckle on March 8, 1946. A roentgenogram on March 11 was negative for fracture. Clinically there was tenderness and thickening of the soft tissues over the metacarpo-phalangeal joint. The patient complained of pain on impact. One-half cc. of amber fluid was aspirated. Adhesive strapping, hot soaks and aspiration brought no relief and on April 12 the bursal sac was excised. Seven weeks later the joint was in excellent condition and the patient resumed boxing.

In mid-November of the same year, this patient injured the knuckle on the little finger of the right hand. No fracture was shown by roentgenogram. The diagnosis was bursitis of the metacarpo-phalangeal joint, right little finger, and ½ cc. of amber fluid was aspirated. Soft tissue over the joint was thickened, and there was pain on impact and tenderness to touch. No improvement resulted from hot soaks, physical therapy and aspiration, and the bursal sac was excised.

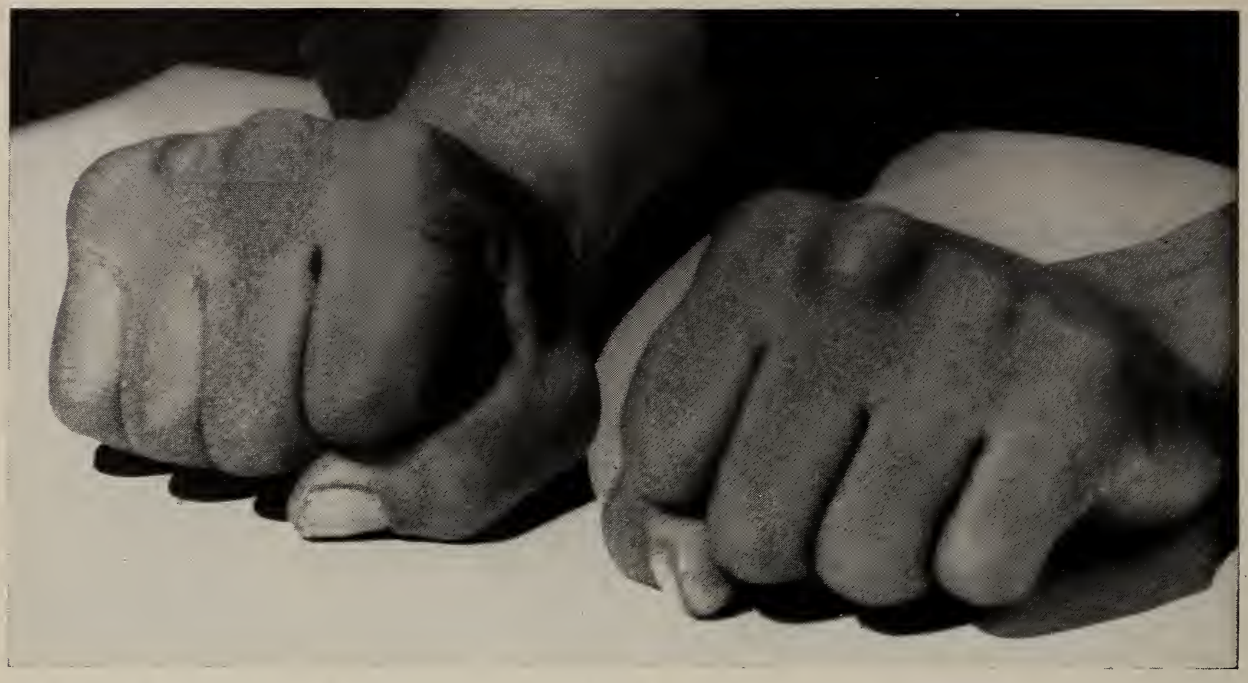


Figure 1.—Right and left hands taken January 17, 1947. Bursal sac left middle knuckle excised April 12, 1946. Right hand shows bursitis of 5th knuckle.

A histological report of the excised bursa follows:

"Reveals portion of a cystic structure composed of dense collagenous stromal wall. There are many blood vessels and slight round cell infiltration. Diagnosis: Bursa."

Four months after the operation the knuckle was apparently sound and the patient resumed boxing.

SUMMARY

1. (a) In a five-year period during which 523 injuries to professional and amateur boxers and wrestlers were treated, traumatic bursitis of the metacarpo-phalangeal joints of the hand was diagnosed in ten instances. (b) The diagnosis of bursitis was confirmed by aspiration of bloody or gelatinous fluid from the affected bursa. (c) The lesion occurred particularly in Negro pugilists following knuckle injuries. (d) Review of the literature indicates that this is a relatively rare disease.

2. These cases were among 22 knuckle injuries treated during the same period, 12 of the 22 (nine in Caucasians and three in Negroes) having been simple contusions which were completely reduced in a few days of treatment with hot soaks.

3. Conservative treatment in seven of the cases of bursitis, consisting of aspiration of the bursa, hot soaks, and adhesive strapping and physical therapy, resulted in clinical cure. In the remaining three the bursal sac was excised and clinical cure followed.

4. Reports of the cases in which the bursal sac was removed are made in detail.

810 South Spring Street.

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Chronic Brucellosis

A Follow-up Study of 133 Patients Treated with Oxidized Vaccine

Joseph Franklin Griggs, M.D., *Claremont*

THE present study reports the results of a follow-up questionnaire returned by 133 patients who had begun treatment with brucella vaccine[9] (usually Foshay's[6] oxidized Brucella abortus or suis vaccine) one to six years previously. Only 13 of these patients had been observed for less than two years; 32 had been observed for two to three years; 77 had been observed for three to five years; and 11 had been observed from five to ten years. The average period of observation here reported is, then, about four years.

Questionnaires were sent to a total of 222 treated patients. The return of 133 is a 60 per cent yield. Questionnaire surveys usually result in a low percentage of returns. A yield of 60 per cent is believed good in view of the length and complexity of the questionnaire and considering the dislocations consequent upon the intervening years of war. The patients were encouraged to report all facts truly and ruthlessly. Replies were received from 34 males and 99 females. The age range was from 9 to 83 years.

Questionnaires were sent to all patients who had received vaccine for longer than two months regardless of whether the diagnosis had been certain or uncertain. The author's criteria for diagnosis have been set forth in previous publications.[10,11] Four categories were established, viz:

1. A definite diagnosis of chronic brucellosis.
2. Probable chronic brucellosis.
3. Possible chronic brucellosis—a doubtful diagnosis—therapeutic test advised.
4. Brucellosis complicated by another disease.

Each patient was informed clearly as to his exact position in this classification before starting vaccine treatment.

RESULTS

Question 1: At the end of vaccine treatment, or when you stopped it, were you improved, () unimproved, () or worse? ()

Answers:	Improved	112	(84.2%)
	Unimproved	18	(13.5%)
	Worse	3	(2.0%)

Analysis: Of the three who were made worse by vaccine one had a doubtful diagnosis, one had a probable diagnosis, and one had a definite diagnosis. The latter was one of the most hyperallergic[9,11] individuals to brucella substances in the author's experience. He was also heavily addicted to barbiturates and had been a severe chronic alcoholic. He was made worse by commercial unoxidized vaccine. The patient with the probable diagnosis was moderately hypersensitive to vaccine and took it for only two and a half months, the shortest period of treatment in the entire series. He then stopped treatment on the advice of "a compident M.D." The patient with the doubtful diagnosis was also hypersensitive to vaccine. The exact nature of her psychosomatic disturbances was never discovered.

Of the 18 patients reporting no improvement, none had been given an undoubted diagnosis of chronic brucellosis. Seven had been given a probable diagnosis. Of these, five were hypersensitive to the vaccine. Five of the seven have either resumed vaccine therapy or have indicated their desire to do so, because they believe that the improvement which they experienced after stopping the vaccine may have been due to the vaccine rather than to the various other non-specific remedies they were using at the time of temporary improvement. In other words, the diagnosis of probable chronic brucellosis remains in five of the seven patients in spite of the apparent failure of the first course of specific vaccine therapy. One of the others was greatly improved by treatment for intestinal parasites. The seventh patient remains unchanged and untreated.

Of the 18 unimproved patients, eight had a doubtful diagnosis of possible chronic brucellosis. One of them also had chronic sinusitis which was probably the primary difficulty, presumably not due to brucella infection. One had a severe mixed type of arthritis concurrently. She resumed brucella vaccine after four years. One was aged, psychotic and addicted to Adalin (bromdiethylacetylcarbamide). One had chronic parotitis, colitis, and severe emotional trauma. One was 83 years old and had arthritis which was improved by Ertron (ergosterol). One resumed brucella vaccine after five years. Two remain unchanged whether treated for other conditions or not.

The remaining three of the 18 unimproved patients had a diagnosis of probable brucellosis with some other complicating disease. One had nasal disease of allergic origin, one had hypertension of unknown origin, and one had a psychoneurosis following severe emotional trauma. The latter was apparently helped by therapy which ignored and denied the probability of brucellosis as a cause of the patient's fever, fatigue, and generalized aching. The other two patients have not been helped.

Of the 112 improved patients, 56 (50 per cent) had been given a definite diagnosis of chronic brucellosis, and ten of them also had complicating concurrent conditions. Only four patients (6.6 per cent) with a definite diagnosis were not improved and three of these had complications. *Vaccine therapy improved 93 per cent of the patients with definite diagnosis of brucellosis who returned questionnaires.*

Because of a small doubt, the diagnosis for 53 patients was "probable chronic brucellosis." Forty-

four of these (83 per cent) reported themselves improved by vaccine therapy, leaving 17 per cent in which the treatment failed.

A therapeutic test with vaccine was given to 20 patients with possible chronic brucellosis whose diagnosis was so doubtful as to be indeterminate. Most of these had only a positive skin test without other objective evidence, or they had no elevation of temperature. Eleven (55 per cent) reported improvement with vaccine therapy. One of these later had the diagnosis confirmed by x-ray findings typical of brucellar spondylitis.[4,12,13,15] Nine (45 per cent) did not respond favorably to vaccine.

Thirteen patients were diagnosed as having chronic brucellosis complicated by some other concurrent disease. Of these, ten (92 per cent) reported benefit from vaccine. The complications in the ten patients reporting benefit were allergy (non-brucellar) in two, psychoneurosis in two, and for the other six, coronary occlusion, cholecystitis, exophthalmic goitre, migraine, endocrine dyscrasia, and sinusitis. The three who were not improved had allergy, hypertension and psychoneurosis respectively.

Question 2: If you were improved, did you give the credit to the vaccine (), or to some other factor(s)? () What other factors, if any? ()

Answers:			
	Credit to Vaccine	89	(80 %)
	Credit to Other Factors	2	(1.8%)
	Vaccine plus Other Factors	20	(18 %)

Analysis: The other factors to which two patients gave all the credit for their improvement were Ertron (ergosterol) in the case of the patient with osteoarthritis, and sanatorium care in the case of the patient who had psychoneurosis after severe emotional trauma. The medications for the latter patient included "thyroid, vitamin B injections, and pills for low blood pressure."

Other factors which 18 per cent of the patients considered important aids to vaccine therapy were: pregnancy, insulin, thyroid extract, bile salts, vitamin B, estrogens, liver, iron, calcium, high protein diet, rest, change of occupation or location, thyroidectomy (for exophthalmic goitre) and pastoral counselling. One patient gave some questionable credit to penicillin. Except for pregnancy, no single factor appeared helpful with sufficient uniformity to make it at all comparable to vaccine.

In relation to pregnancy as an aid to vaccine therapy it is interesting to compare the fact that in *untreated* brucellosis pregnancy is detrimental to the patient. Each succeeding pregnancy, even if carried to term, leaves the untreated patient more depleted of strength and health. But if vaccine is administered throughout the gestation and lactation periods, recovery from brucellosis is usually accelerated and pregnancy appears to be an advantage. One patient was apparently cured for three years but relapsed after two pregnancies without vaccine, one of which aborted. Vaccine safeguards the fetus and also transforms the pregnancy from a detriment into an advantage to the mother. This synergistic effect of treatment and pregnancy in brucellosis is analogous to the same phenomenon well known in syphilis, another common chronic granulomatous infection.

Question 3: If you were made worse during treatment did you think the vaccine was responsible (), or some other factors? () What other factors, if any?

Answer: This question was answered by the three patients who were made worse by vaccine and by about 20 per cent of the others who were temporarily so hypersensitive to the vaccine that they suffered from reactions until the dosage was very radically reduced to their tolerance. This undesirable effect was much more frequent when unmodified commercial vaccine was employed. Oxidized vaccine[6,9] is much safer to use on patients with marked allergy to brucella substances.

Question 4: How much of a cure did the vaccine bring about in your case? A (), B (), C (), D (), E (), F (), G ().

The answers to this question are shown in Table 1.

Analysis of answers to Question 4: As in any questionnaire, discrepancies can be found between the answers to this question and the answers to

TABLE 1.—*Answers to Question 4*

Answers	Degree of Recovery	Number of Patients	Per Cent
A.	"More than 100% cure or better health than I had ever known in my life before"	6	4.6%
B.	100% or complete restoration of former good health	12	9.2%
	Total Complete Recovery	18	13.8%
C.	Not complete return of constant health and energy but marked improvement, or loss of disability, a "very good" result	36	27.6%
D.	A "good" result: "better than for some years" or "somewhat better in every way" or "definitely better in certain important ways" or 30% to 80% improved. The average per cent mentioned by 25 patients in this group was 60.3%	37	28.4%
E.	Only a fair result: Definite improvement but only temporary and never very complete in any important respect. Could not tell whether the improvement was due to the vaccine or to the natural undulations of the disease, although it seemed at the time to be the vaccine	17	13 %
	Total Improved but not Cured	90	69.2%
	Total Improved	108	83 %
F.	No effect from the treatment at all. A waste of time and money as far as the results are concerned. Or, "the treatment seemed to make me feel sometimes much better and sometimes much worse than usual"	17	13 %
G.	Poor results: the treatment was consistently and finally disadvantageous	5	3.8%
	Total Unimproved	22	16.9%

Question 1. For example, two patients, a mother and daughter, answered this question by checking answer G, indicating disadvantageous results of treatment, but they answered Question 1 by checking "unimproved" and did not indicate "worse." These patients were both hypersensitive to vaccine so tolerated it poorly, but their final condition was certainly not worse because of it. Discrepancies of 1 or 2 per cent are not significant differences.

Analysis of those who recovered completely shows two factors of interest and significance. One is age; the other is the degree of sensitivity[9,11] to brucella vaccine. Of the 18 who considered themselves cured, three were under 20 years of age, seven under 30, 14 under 40, and all but two under 50. These two were a man aged 71 who had had acute brucellosis and had once before recovered quite well, and a 75-year-old woman who stopped vaccine after two years because she felt cured. She had been given a diagnosis of probable chronic brucellosis. It is unusual for such old persons to recover completely. Neither of these two aged patients was hypersensitive to the vaccine. Only three of the 18 who recovered completely were hypersensitive to the vaccine, and in all three the hypersensitivity was overcome[9] in the early stage of treatment.

The shortest period of follow-up in the completely recovered group was one and a half years and the average period of observation of this group was 3.6 years.

Analysis of the group of patients who did not improve shows the incidence of hypersensitivity to be 50 per cent of the entire group and 67 per cent of those in the group which had a definite or probable diagnosis of chronic brucellosis. The average age of the unimproved group was 50 years while 89 per cent of the recovered group were under 50 years of age. The longest period of treatment in the unimproved group was two and one-half years and the average length of treatment was only nine months.

This study tends to confirm an impression that the unfavorable factors in the prognosis of chronic brucellosis are brucellar allergy,[9,11] advanced age, duration of illness,[11] ineradicable foci and other complications.

Question 5: Did your improvement appear during vaccine treatment () or not until after you had stopped it? ()

Answers:	During vaccine treatment	97	(86.6%)
	After vaccine treatment	4	(3.6%)
	Both during and after vaccine treatment	11	(9.8%)

Comment: This finding is in contrast to the general impression that improvement often does not appear until vaccine therapy has been discontinued or completed. Such an impression results from the use of large doses of unmodified vaccines which often cause undesirable reactions.

Question 6: Were you hypersensitive to the vaccine? Did it seem too strong for you? At first only? Toward the end of the course? All the time?

Answers:	Not hypersensitive (patient's judgment)	76	(57.6%)
	Hypersensitive at first only (author's judgment)	30	
	Hypersensitive toward end of course (author's judgment)	13	
	Hypersensitive all the time (author's judgment)	30	
	Total hypersensitive (author's judgment)	73	(55.3%)

Comment: When hypersensitivity is severe it is obvious to both patient and physician. It is manifested by necrotic or near-necrotic local reactions to intracutaneous or subcutaneous injections, usually a generalized systemic reaction, exacerbation of symptoms, and an increase in sensitization if such treatment is continued. Lesser degrees of hypersensitivity may be obvious only to the physician because the size of the dose of vaccine which he administers is all-important and is usually known only to the physician and not to the patient. Thus in the answers above there are 17 patients who reported themselves not hypersensitive to the vaccine but who, in the physician's judgment, manifested or developed hypersensitization at some stage of the treatment.

Patients are considered hypersensitive or allergic to brucella when: (1) local reactions to skin tests persist for longer than four months or cause ++++ reactions with necrosis or near-necrosis; (2) vaccine injections of several thousand killed bacteria cause generalized constitutional reactions with exacerbation of symptoms; (3) the size of the dose of vaccine cannot be increased without increasing the patient's symptoms and reactions; (4) the local reactions to tolerated doses of vaccine persist longer than four or five days; or (5) evidence of hypersensitization increases as vaccine treatment is continued. The prognostic and diagnostic significance of brucellar allergy is discussed in the analysis of Question 4 and in other publications.[9,11] The avoidance of hypersensitization is almost a prerequisite to successful treatment.

Question 7: How long were you treated with vaccine to the best of your memory? Which year or years?

Answers:	Shortest treatment	6	weeks
	Longest treatment	9	years
	Average treatment	1½	years

Comment: The longest treatments were not usually continuous but intermittent. Only 19 patients (14 per cent) were treated for less than six months. When treatment is to be successful some improvement is usually noticeable within two or three months after starting vaccine therapy by our present methods.

Question 8: Did you give vaccine to yourself (), or was it always administered in my office (), or by some other doctor () or nurse ()?

Answers:	Always administered in my office	57	(43 %)
	Self-administered after starting in my office	50	(37.6%)
	Self-administered or by other doctor or nurse	75	

Comment: Answers to this question were so variously combined that an orderly analysis is impossible. However, the significance of this question is

seen in the fact that because of the dislocations incident to the war, more than half of the patients had to administer their own vaccine or have it done by persons other than their attending physician. The initial strength of vaccine and principles of dosage were determined for each patient by the author and most of the subsequent changes were advised by mail or long distance telephone. The suggestive effect of the doctor's presence was thus eliminated. Of those who recovered completely, only 39 per cent were treated by the author exclusively while 52 per cent of the unimproved group were treated by the author exclusively. In relation to the whole series these figures show no significant difference.

The possible suggestive effect of administering one's own injections is not entirely ruled out since 44 per cent of the recovered patients state that they injected the vaccine themselves at least part of the time, while only 14 per cent of the unimproved group gave themselves the injections. However, it is doubtful that patients would continue such a troublesome and unpleasant procedure for an average of one year and ten months if the effect were purely suggestive. Intimate knowledge of the behavior of patients in such cases gives the impression that the unimproved patients did not give themselves injections because they had not improved after the first few weeks under the doctor's care.

Question 9: Which of your symptoms was most completely relieved by treatment?

Question 10: Which symptom has been most persistently troublesome in spite of treatment?

Answers to these questions are shown in Table 2.

Table 2.—*Answers to Questions 9 and 10*

Symptoms	Most Relieved	Most Persistent
Weakness, exhaustion, fatigue, lack of energy, malaise	49	32
Aching, lameness, arthritic pain, neuralgia, myalgia	42	27
Chest pains	3	0
"Muscular tension"	0	1
Eyestrain, burning of eyes	1	2
Nervousness, irritability, instability, depression, apathy	16	6
Insomnia	4	4
Fever	14	10
General condition, undulations, general health	14	2
Intestinal distress, indigestion, diarrhea, nausea, colitis, constipation, peptic ulcer symptoms	14	20
Heachache	9	13
Light-headedness, dizziness	5	2
"Buzzing in head"	0	1
"Can't think clearly"	0	1
Rapid heart, palpitation, "heart" attacks	9	3
Paroxysmal auricular fibrillation	0	1
Frequent feelings of a cold, "flu," sinusitis, allergy, asthma, sore throat	7	10
Nasal crusts	0	1
Urinary frequency, cystitis, Hunner's ulcer, pelvic pain, dysmenorrhea	6	2
Sterility	1	0
Pain in RLQ, postoperatively	0	3
Abortion	0	1
"All symptoms"	5	1
Night sweats	4	1
Weight loss, emaciation	3	0
Skin eruptions	1	3
Iritis, edema, hypertension	each 1	0
Hyperthyroidism, foot-drop, arteriosclerotic aphasia	0	each 1
Questions not answered	25	36

Comment on answers to Questions 9 and 10: The array of symptoms will tend to discredit the concept of chronic brucellosis as a clinical entity unless one is familiar with the protean nature of its manifestations and with its behavior as an allergenic,[5,9,11] intracellular,[1,8,16] granulomatous[14] and generalized chronic infection. The diagnosis cannot be made on the basis of symptomatology[2,3,11] because brucellosis is another "great imitator," surpassing even syphilis in this respect. It should be noted that the symptoms here mentioned do not constitute a complete list of the symptoms presented by these patients.

There are few important differences between the answers to Questions 9 and 10. Many patients listed the same symptoms in answer to both questions. However, a great many of them indicated a marked decrease in the frequency, severity, or duration of the symptoms which still persist. The "rheumatic" symptoms and general languor are the ones most likely to be improved by vaccine. The persistence of intestinal symptoms may be interpreted to suggest that the most common focus of brucella infection is in the alimentary tract, the portal of entry in practically all the cases here reported. However, it may also be an expression of the frequent coexistence and confusion of psychosomatic disorders with chronic brucellosis. Nervous symptoms in brucellosis respond well to vaccine therapy except when there is an important psychogenic component. As in other encephalitides, headache and dizziness are often stubborn symptoms. The persistence of "cold" symptoms is probably a reflection of the allergenic nature of brucella substances.

Question 11: When you stopped my vaccine treatment did you stop because I so advised (), or for other reasons? () What other reasons, if any?

Answers:			
	Continued taking vaccine	20	(15%)
	Stopped taking vaccine on author's advice	52	(39%)
	Stopped for other reasons	61	(46%)
	Resumed vaccine after stopping it	37+	(32%+)

Those patients who stopped vaccine without my advice gave the following reasons:

Patient or doctor moved due to the war	32
Patient seemed cured or much improved	11
Because of excessive reactions	8
Because of lack of improvement, or relapsed during treatment	7
On other doctor's advice	4
Doubted diagnosis	2
Expense	1
Carelessness	1

Question 12: Did you get worse again after you stopped taking vaccine?

Answers: Continued improvement was indicated by 56 patients or 50 per cent of those replying to

this question. Some degree of relapse is known to have been experienced by 55 (49 per cent) of those who reported some improvement. However, most of them indicated that their condition in relapse was mild compared to their condition prior to vaccine therapy. Vaccine was resumed by at least 37 (67 per cent) of this group of 55. In the group of patients who reported themselves 100 per cent recovered, the relapse rate was 22 per cent. Only one of these required more than a few injections of vaccine to regain normal health. In the group of patients given an undoubted diagnosis of chronic brucellosis, the relapse rate was as high as 42 per cent if we count as relapsed all patients who resumed vaccine therapeutically even for one dose. By the same arbitrary criterion the relapse rate was 28.5 per cent in those with a probable diagnosis of chronic brucellosis. This questionnaire provides no method of determining a significant rate of relapse and degree of relapse in chronic brucellosis. It does confirm the impression that chronic brucellosis is a disease existing usually in a rather fine balance with the body's resistive powers[7, 9] and therefore prone to relapse.

Question 13: Meanwhile have other M.D.'s given you different diagnoses? If so, what? Has treatment for any other conditions cured you of any symptoms which I thought were probably due to brucellosis? If so, what symptoms? How long have any such symptoms been cured?

Answers: Only ten patients had received a different diagnosis from other physicians. One of these was improved by Ertron (ergosterol), one by desensitization to her allergens and by eye exercises for poor fusion (she had already received a "very good result" from her brucella vaccine and was referred to an allergist), one was greatly helped by psychotherapy in a sanitarium after only "fair improvement" on vaccine, one was "cured of extreme pain, fatigue, and nervousness by vitamins, thyroid, pills for low blood pressure, and reassurance that she had no brucellosis," and one was helped by suprarenal cortical extract orally for colitis but she later resumed brucella vaccine. The other five patients mention no symptoms which were relieved by therapy for the various other diagnoses they were given. The other diagnoses are unknown in four cases. One of these patients also later resumed brucella vaccine. The tenth patient was a woman 75 years old with a diagnosis of "maladjustment to life."

Four patients were improved by surgical operations, viz: thyroidectomy for hyperthyroidism, radical operation upon the sphenoids for severe sinusitis, and appendectomy in two cases of pain in the right lower quadrant of the abdomen.

Other effective therapies were reported as follows: colitis cured by Manson-Bahr combined therapy for amebiasis; sinusitis improved by penicillin; nervousness improved in two patients by estrogens; anemia by "blood-building shots"; depression and fatigue improved by rest and hormones; "gall bladder" symptoms by ulcer therapy; and colitis by Sansum's concentrated pancreatic extract. One patient thought that ethylene disulphonate helped to relieve his hypersensitivity to brucella vaccine. Another thought he was better when vitamin B was added to his vaccine. Thyroid, radionics, pregnancy, and psychological outlook were praised by one person each, but not in relation to any particular symptom or diagnosis other than brucellosis.

The following symptoms were mentioned as cured or improved by other means but the particular therapeutic agent was not reported: arthritis, conjunctivitis, digestive symptoms, irregular menses and low blood pressure, anemia and weight loss. No patient answered the question, "How long have such symptoms been cured?"

In summary, a variety of other therapies are given some credit by 30 patients in this series (22 per cent). It appears that such therapies are efficacious chiefly when there are important complications or when chronic brucellosis is not the correct diagnosis, because the same measures have been tried repeatedly in many cases of chronic brucellosis with little or no result. The answers to this question clearly indicate the need for as complete a diagnosis and treatment as possible in every case of chronic illness.

Question 14: Have other doctors treated you for brucellosis (undulant fever) with vaccine since you stopped treatment with me? Remarks:

Answers: Of 65 patients who consulted other physicians, 35 (54 per cent) were again given a diagnosis of brucellosis and were treated accordingly. The others are analyzed under Question 13. Of the 35 treated for brucellosis, two were given typhoid shock therapy but made no mention of its effectiveness. One of these is known to have resumed brucella vaccine later. The remaining 33 all received brucella vaccine in various forms.

Question 15: At the start of your vaccine treatment with me, was it your impression that the diagnosis of chronic brucellosis in your case was certain (); or probable, though tests were not conclusive (); or so uncertain that we needed to observe the results of treatment before we could decide (); or complicated by some other trouble at the same time ()?

The answers are shown in Table 3.

Comment: In Table 3 each patient's answer has been compared with the author's impression which was written on the patient's office record before treatment began. Of the 47 patients given the certain diagnosis of chronic brucellosis practically all recollected the diagnosis correctly. Only one thought that there had been serious doubt of the diagnosis. Of the 20 patients in whose cases the doctor was seriously in doubt, 70 per cent recollected this fact correctly. But in the group of 53 given a probable diagnosis, 23 (43 per cent) jumped to the conclusion that the diagnosis had been an undoubted one. Thus it appears that it is more difficult for the mind to maintain a small degree of doubt than it is to entertain either certainty or a large degree of doubt. Since

TABLE 3.—*Answers to Question 15*

	Doctor's Diagnosis	Patient's Recollection	Doctor's Diagnosis	Patient's Recollection	Doctor's Diagnosis	Patient's Recollection	Doctor's Diagnosis	Patient's Recollection
Certain	47	42 (89%)		23 (43%)		3		5 (39%)
Probable		2 (4%)	53	19 (36%)		0		0
Uncertain		1 (2%)		7 (13%) None 1	20	14 (70%)		1 (7%)
With Complications		2 (4%)		3 (6%)		3 (15%)	13	7 (54%)
Totals	47	47	53	53	20	20	13	13

83 per cent of the group diagnosed as probably having chronic brucellosis improved on vaccine therapy it is likely that the patient's impression reported in answer to Question 15 is not a true recollection in many cases, but a conclusion as the result of subsequent favorable treatment with brucella vaccine.

DISCUSSION

A great many different substances have been reported as therapeutic agents for undulant fever. Harris[12] listed 20 in 1941. New ones are hailed in the hopeful press every few weeks or months. The author has tried 25 treatments during the past ten years in cases of chronic brucellosis.

In acute undulant fever the value of any treatment is difficult to assess because sudden spontaneous remissions are a part of the natural course of the acute form of the disease. Apparently many substances are capable of provoking such a remission. However, none can be counted upon or tolerated in every case. This tendency to ultimate spontaneous cure of the acute disease led to the erroneous impression that undulant fever is a self-limited disease. We now know that many acute cases become chronic in a low-grade form and that many more chronic cases appear without having passed through any recognizable acute stage. Consequently it appears that acute cases should be vigorously treated with immune blood, plasma, or immune globulin, streptomycin, and sulfonamides.

Chronic brucellosis is a far more difficult problem in therapy. Like the other chronic infective granulomas, such as tuberculosis, syphilis and leprosy, chronic brucellosis cannot be cured quickly and with certainty. The causative organism, brucella, usually prefers an intracellular[1,8,16] existence; and when it is well established in its host, it is not vulnerable to the antibiotics, agglutinins, and phagocytes which the blood stream may be induced to contain. Consequently the treatment of chronic brucellosis has been singularly disappointing. The present consensus is that the host can only be stimulated to resist the invader more actively with its own mechanisms, or it can perhaps be induced to tolerate the parasite more comfortably. The first objective has been attempted by means of specific and non-specific shock therapy. The second objective has been sought through non-specific tonic measures (liver extract, vitamins, etc.) and by specific desensitization with very small doses of brucella vaccines and similar derivatives. In both approaches the removal of active foci is advocated when possible.

The author's method of treatment has been reported in previous publications.[9] Some of the cases reported in the present study represent the earlier experimental period of vaccine therapy before we fully appreciated the importance of avoiding hypersensitization. These results, therefore, can be said to apply only to specific vaccine therapy in general; not to any particular refinement of it.

SUMMARY

1. A questionnaire was answered by 60 per cent of 222 patients who had been treated with oxidized brucella vaccine.

2. The average period of treatment was one and one-half years. The average length of observation of all cases was more than four years.

3. Improvement was reported by 84 per cent. Three patients reported that they were made worse by vaccine. The remainder (13.5 per cent) were unimproved. None of the latter had been given an undoubted diagnosis of chronic brucellosis.

4. The patients were classified as to the degree of certainty of the diagnosis before treatment was begun. The questionnaire is analyzed so as to show the effect of treatment in each classified group. Success in treatment appears to be correlated to certainty of diagnosis, but this does not imply that a therapeutic test is entirely reliable in diagnosis.

5. Therapeutic factors other than vaccine are studied but they do not appear to be of much importance in this series of patients, except to call attention to the importance of completeness in the diagnosis and treatment of chronic illness.

6. A study of the degree of improvement achieved shows that only about 14 per cent recovered completely, 28 per cent reported a "very good result," another 28 per cent a "good result," and 13 per cent only a fair improvement.

7. Unfavorable prognostic factors in chronic brucellosis are extreme hypersensitivity to brucella substances, advanced age, long duration of the illness, inaccessible brucellar foci and other complications.

8. About half of the patients manifested rather severe hypersensitization to brucella at some stage of their course. This manifestation is described. Its avoidance during diagnosis and treatment is important to success.

9. Self-administration of the vaccine by intelligent patients is quite feasible after the first few weeks or months of the physician's instruction and dem-

onstration. The factor of suggestion is examined in this study.

10. The individual symptoms most responsive to therapy, and the most persistent symptoms in spite of therapy are tabulated. The diagnosis of brucellosis cannot be made or excluded on the basis of symptomatology.

11. While the degree of relapse was relatively slight, the rate of relapse in the different groups of patients in this study varied between 22 per cent and 49 per cent.

12. The diagnosis of chronic brucellosis was rather well supported by other physicians who saw about half of these patients.

13. A study is made of the patients' reliability in remembering the exact diagnoses which were given to them.

14. Because of the limitations of any questionnaire survey, conclusions which may be drawn from these replies must be held as only tentative. This study appears to support the view that chronic brucellosis is a complicated disease entity which is difficult to prove and which is worthy of careful treatment with vaccine until a more effective agent is discovered.

1011 Berkeley Avenue.

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Mental Health in the Public Health Program

KENT A. ZIMMERMAN, M.D., *San Francisco*

THE specialties of pediatrics, public health, and neuropsychiatry are making significant contributions to the field of mental health. The subject of this presentation is ways in which these three specialties can be interrelated to produce a potentially important contribution to the practice of medicine.

It is everyone's fervent hope that more and more mental hygiene clinics and more and more psychiatrists, psychologists, and psychiatric social workers will be with us soon. However, we will get no real concept of our total mental health need if we think only of specialized treatment facilities and specialists to man them. We badly need psychiatric clinic facilities, expensive though they may be. Even though the annual cost of a child guidance clinic or a psychiatric clinic is twenty to thirty thousand dollars these days, many communities have some or all the funds necessary for one clinic or more. The great limiting factor at present is the lack of highly trained personnel to staff these clinics. One authority has estimated that the country needs a minimum of 10,000 more psychiatrists. Few people realize, however, that with present training facilities it has been estimated that it would take 100 years to train this number.[2] Obviously, our people won't quietly wait this length of time for this number of specialists to be trained.

At the present time people have become much interested in emotional disorders. We seem to be going through a cultural cycle in which our films, our literature, and our citizen group discussions reflect an intense preoccupation with the warped personality and the mentally ill. This is not without significance for medicine, for with the awakening of such public interest it is only natural that its impact will be felt by the physician in practice. Many physicians have an increasing number of patients with emotional problems coming to their offices. The pediatrician, especially, has felt a need to be aware of the emotions that mothers and children bring to his office. It has long been a maxim in pediatrics that a doctor does not deal with one patient when he sees a child, but he always has at least two, since a parent is usually in the picture—and sometimes three, when the grandparent is also on the scene. And the pediatrician understands that the treatment of the extra one or two patients in this situation almost always primarily consists in helping the parents handle the emotions that are aroused by the illness of the child.

Even if we had all the psychiatric clinics we needed, and the personnel to staff them, we would probably not solve our problem. If more clinics were available, more and more people would develop an understanding and acceptance of psychiatric treatment and the demand for treatment would mount proportionately. It seems, then, that there should be another approach made toward meeting some of our mental health problems at a different stage of development. Our patients want help with their emotional problems before they reach the stage where specialized treatment is necessary. They are demanding this help in our offices and clinics, and we should be reminded that it has always been the demand of the patient that in the long run has shaped the practice of medicine.[3] Increasing the number of psychiatric clinics and psychiatric personnel will not alone meet this need.

PSYCHIATRIC KNOWLEDGE APPLICABLE IN GENERAL MEDICINE

We may safely say that psychiatry can now offer a body of knowledge which can be applied to general medicine. Investigations and research on the development of the human personality have produced some facts and much theory—which is workable—which can be applied as part of the medical care in office and clinic practice. Although we know, in general, very little about the development of the human personality, we can say with some confidence, from the results of studies and knowledge uncovered by psychiatric techniques, that the period of childhood is one of the most important, as far as the individual's ability to develop healthy personality adjustment patterns is concerned. We do know that the family and the emotional relationships between the parents, and between parents and child, are also important in the development of the growing individual's pattern. Likewise, we know that mental health is not something to be attained once and for all. Mental health, in the final analysis, is the individual's ability to maintain a more or less constant adjustment to constantly recurring stimuli in the environment which tend to upset this adjustment.

Certain experiences in the life span of individuals affect some persons more than others, just as does an episode of infectious disease affect the body economy of some individuals more than that of others. Psychiatry has been able to pick some of these life experiences out and identify for us some of the emotional forces involved. Beginning in infancy, the matter of feeding and weaning, toilet-training in early childhood, the growing separation from, and independence of, the mother, are significant emotional experiences. The nursery school and elementary school as first attempts at integration with the group; adolescence, marriage, and the time of the psychological acceptance of aging, are some other points at which individuals are called upon to make a greater adjustment than usual.

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In addition to these common life experiences, we all are beginning to realize that certain types of illness play a most important role in the developing personality. The child who needs prolonged orthopedic care, with removal from the home for a period of time, is especially vulnerable, and needs psychological support. The breadwinner who is suddenly confronted with the fact that he has tuberculosis and needs to go to a sanitarium, presents a situation where not only the individual needs psychological support, but so does the rest of his family. Death and divorce in a family bring other crises that many individuals are called upon to handle. Anyone who is in medicine, be he physician, nurse, or social worker, has daily experience with this. Those of us in public health are called upon to handle large numbers of the types of illness that demand long care or about which the public feels very keenly, as, for instance, the venereal diseases and the diseases which come under the crippled children program.

The development of pediatrics in this country has contributed largely to the great growth of our preventive medical services to mothers and children. One can easily say, as he visits well-baby clinics over the country, that a relatively good job is being done in checking on the growth and physical development of large numbers of our infants and pre-school children. However, in many places the public feels that this check on the physical aspect of growth is not enough. The size of the output of books on motherhood and baby care and family life is a significant sign of our times. The great search for this kind of knowledge and for a strengthening and reassurance of motherhood and parenthood is a reflection of change in our family and community life. A large part of this need undoubtedly originates in the inadequate way our communities train our young men and young women for the art of parenthood. It might also be considered a result of lack of preparedness of the medical profession in being able to meet the needs of parents in this respect. Whatever the cause, it remains a fact that new mothers with new babies bring to the general practitioners' and the pediatricians' offices and clinics, along with their babies, emotions which they want some help in handling. The new mother feels, rightly, that motherhood is a test of her as an individual. She feels that she is being judged by her mother, by her in-laws, by her husband, by the neighborhood, and by her physician. She not only comes for medical direction, but she also seeks support from the physician in her job as a mother. If in addition to these natural feelings of insecurity she has, for example, some conflict about having the baby, she brings to the office or clinic an attitude which often baffles and sometimes irritates the physician and nurse who see her. When she meets this response, the new mother becomes, therefore, more confused, more unsure of herself—all of which is reflected, usually, in the care of the baby; and trouble begins to appear.

Persistent feeding problems, in such a situation, are likely to arise; problems in the management of the baby at home in relation to the rest of the family; later on, difficulty about toilet-training; and still later on, difficulty in the child leaving the parents to mix with the play group in the neighborhood or school. If this mother gets no early help, often the problem becomes acute enough so that the specialized help of a child guidance clinic is required, and another "problem child" is in the making.

The problem that we face is, first, what can we who work with and offer services to mothers and children do to recognize some of these problems; and, second, how can we help such a mother to handle disturbing emotions that exist between herself and her child.

KNOWLEDGE OF NORMAL EMOTIONAL GROWTH NEEDED

We might list some of the areas in which greater knowledge and understanding would help us to appreciate more fully the growth and development of children and adults. Certainly we need to know as much specific information as is available about normal growth and development. Much of this material, as far as physical growth goes, is in the standard textbooks. What is lacking is knowledge about normal emotional growth and development. This is easily seen, perhaps, in our own experiences, when we recall that some of our most difficult patients to be dealt with in our offices were the "normal." Our lack of knowledge about the normal makes us prone to feel uncomfortable when we have a patient to talk to whose make-up is more or less along normal lines. This is natural, since our training and education have been in terms of the abnormal. But more knowledge about emotional growth and development will not be enough. It is the way knowledge is applied to the patient that seems to be the other important subject which is missing in our medical education.

Through studies of the therapeutic relationship in psychiatry, it is revealed as important for us to know and recognize certain reactions in our own personalities (and this is true of everyone) which block us from helping some of the patients who confront us. Many of us are made uncomfortable by certain kinds of emotions which patients bring to us as part of the picture of their illness. To some of us, the aggressive, demanding patient, the angry patient, is upsetting. In other cases, the indifferent patient creates antagonism in some of us, and we reflexly make moral judgments under our breath about him, such as: "No sense of responsibility!" or "Lazy good-for-nothing!" Many of us, as we try to handle the emotions of these patients, do so through mechanical means and through certain defense mechanisms of our own personality. Many times, we will offer medicine, not so much for its chemical properties, but more because of its psychological value—not only to the patient, but also for the physician. We will sometimes unconsciously talk so much that we prevent the patient from being able to talk and thus make us uncomfortable; or we deliberately avoid giving the patient a chance to touch on the subject we sense he most wants to talk about. We do this, it seems to me, because we are lacking instruction and guidance in

how to use another therapeutic tool that all of us have but that all of us would like to use more skilfully —that is, the art of interviewing and talking to patients, and the realization that our personalities are powerful therapeutic agents or irritants.

All of the foregoing is stated not in a spirit of criticism, but with a desire to determine what needs should be met to make us more effective as healers. Medical and nursing education is always incomplete. When we graduate from medical schools, and when we complete our residencies, we all accept the condition that we will learn further from the patients who seek our help. And it is becoming apparent that it is in the skill of understanding, accepting, and handling the emotional component of the problems of growth and of illness that patients bring to us that we need to learn most.

We are gradually becoming aware, too, that the use of such skill in dealing with these common emotional experiences is the basis of prevention of later more serious emotional disturbances. A few examples will illustrate this. The pre-natal clinic is one to which pregnant women bring many emotions along with their pregnancies. Rather often one meets women who use the clinic to see if it is possible to terminate pregnancy. The physician is not infrequently confronted with the request, "Doctor, can I have an abortion?" This question usually makes a physician or nurse become cold in manner, cautious, wary, often authoritatively disproving, and he stops further conversation about the matter. Often, this reaction makes the patient feel more guilty and inferior, and thus blocks the building of a good patient-physician relationship at the very time it is most needed. Many physicians know that by helping a woman talk about such a problem, she can be given enough psychological support to work her problem through without risking the consequences of a visit to an abortion mill.

On one occasion the author saw in a pediatric clinic a mother and her third and youngest son, who had been moderately crippled by poliomyelitis. In the course of the conversation the mother was complimented on her constructive attitude toward her son's handicap. She said, "Yes, a visiting nurse helped me get that. For the first year after Bobby's attack, I gave all my time and thought to him. My husband and two other boys were neglected, although I really didn't realize it. One day, my second boy brought a note home from the teacher. They wanted to send him to a school guidance department. I got scared. The visiting nurse called that week and I talked it over with her. She helped me see I hadn't given enough attention to the others, and then I woke up and saw what was happening. My son didn't have to go to the clinic, and Bobby did better when I didn't give him so much attention."

In a well-child clinic, on another occasion, a mother came who wanted advice about a bowel-training problem in her three-year-old child. The history indicated a good deal of coerciveness, rigidity, and frustration over her inability to "get her trained." Quite in contrast was the fact that with her older child, a boy, her approach to bowel training had been much more permissive, and without the element of anxiety that colored her attitude toward her second child. At one point she said, "Oh, if I only felt about this child like I did toward my first!" Pursuing this lead, it became apparent she had some disturbing feelings over the fact that her first child was her favorite. In respect to this she said, "Doctor," I feel I just have to do more for this second child. I owe it to her." Over the next three visits, short therapeutic conversations were successful in helping her talk about her guilt feelings, and to accept them and handle them. The results were a lessening of pressure on the child, and the bowel problem disappeared within a month. She said then, "You don't know how much better I feel. And Janice [her daughter] feels so much better about me. She seems a different girl."

These instances seem to demonstrate that simple, but artful therapeutic relationships can be "preventive" in the sense of reducing suffering by reducing the hazard of more serious deviation from the normal, and by reducing the need for probable specialized medical attention at a later date. It is also "preventive" in the sense that we promote the general health of the patient. This is certainly one of the aims of medicine.

POSTGRADUATE EDUCATIONAL NEEDS

In the State Department of Health we wish to explore what is needed in the way of post-graduate education to give physicians and nurses in public health work the knowledge and practice which will help them meet the emotional needs of their patients. We believe there are two main kinds of information and practice, which, if supplied over a period of time, give promise of enabling us to grow professionally in this way.

1. More concrete knowledge about the patient-physician relationship. This implies a concept of the mechanism of this relationship, and the concept of controlled emotional change during the relationship. Whether we are aware of it or not, each patient is changed emotionally by his therapeutic experience with a doctor, and each patient alters the personality of the physician. Psychiatry has given us greater understanding about this, the rapport or transference: it is one of psychiatry's great contributions to medicine.

2. A certain body of knowledge about the development and functioning of the human personality. Some of the points to be emphasized would be:

(a) Development of the normal personality in child and adult.

(b) A sick person is different emotionally from a well person—and in what way.

(c) The types of conflict that produce anxiety.

(d) The common devices for handling anxiety, such as nightmares, superstitions, phobias, etc.

(e) Common psychopathology—with a knowledge of the healthy and unhealthy defense mechanisms such as rationalization and projection, etc.

(f) The classic types of emotional illness.

(g) The biological-social interplay between members of a family that determines emotional growth of the family as a unit.

(h) The influence of the neighborhood and its relation to the personality.

Of equal importance with the content of such instruction, is the question as to how this material can be made a part of a health department staff. Lecturing on these subjects is not the complete answer, for in general the material does not become integrated to one's practice. Some knowledge can be taken from the field of social work training, where an experienced individual guides the student worker in the analysis of the patients' and the students' emotional interplay as it develops during the handling of a series of interviews. A teaching psychiatric social worker, or psychiatrist, added to the staff might accomplish this. A lesson may also be taken from the experience of the cooperative nursery school movement. As you know, mothers help take care of the children under the teaching-direction of a good head nursery school teacher. In this way great insight is gained in a relatively short time when one is working with children at a stage in their growth when their behavior reveals the raw emotion of developing conflicting elements of personality structure at its simplest. Nursery school experience for a few well chosen nurses and physicians for several months would give them greater understanding of child behavior and development and prepare them to better care for the individual that is sick or has a problem. Another kind of educational experience that could be tried would be the experiment undertaken by the University of Minnesota and the Commonwealth Fund in their two-week training of 30 general practitioners to handle the psychoneurotic patient in their offices more satisfactorily.[1] This seems to have been rather successful, and might well be attempted with selected groups of public health physicians and nurses.

Since we do not know any final answers to these problems, an exploration and study will first be made by way of one or more demonstrations in selected local health departments. It is also planned to offer a course in mental health concepts of growth and development for members of the administrative and consultative staff of the State Health Department, so that the influence of this knowledge of growth and development may be incorporated in the planning of programs.

TRAINING FOR PUBLIC HEALTH WORKERS

We also contemplate providing some sort of training situation in which public health workers in local areas may be given an opportunity to take special concentrated courses in growth and development as this is related to the problems of public health medicine. We are thinking in this respect of utilizing the knowledge and the teaching experience which the nursery school and a good nursery school staff could bring to this problem. The aims of our training would not be to create specialists, but rather would be that through this training the individual might return to his local health department with a better understanding and a clearer vision of what some of the implications of his practice are in relation to the mental health of the growing personality.

541 Phelan Building.

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Discussion by OSCAR REISS, M.D.

Medicine is ever expanding its scope of knowledge concerning health, and with it comes a better understanding of measures necessary for the prevention of sickness.

In no special branch of medicine are the opportunities for practising preventive measures greater, or more important, than in the field of pediatrics. Time was when the accent was on disease; now it is on health, with striving for optimal health. And with this our definition of health has broadened to include not only the physical, but also the emotional and mental well-being of the individual.

During the past 20 years an ever-increasing number of parents have become aware of the benefits of pediatric supervision of the well child from the day of birth, so that today the care of the well child occupies perhaps the major part of the pediatrician's time. His attentions to the child have become largely focused on physical growth and development, on the correction of remediable defects, and on the institution of measures for the prevention of infection. Not a great deal of attention has he paid to the establishment of mental hygiene. Partly because of this, his little patients develop behavior difficulties, many of which could have been prevented, but which offer formidable resistance to correction, and may even leave their imprint for life.

If the pediatrician hopes to remain prominently in the picture, the scope of pediatrics must broaden to the point where its disciples attain a comprehensive understanding of every phase of child welfare, and qualify themselves as authoritative in all its aspects.

Life grows more complex daily; the tempo quickens constantly; and emotional strains grow greater. Mental hygiene becomes increasingly more important.

The role for which the pediatrician must prepare himself is that of a potent environmental force, acting both directly and indirectly—directly, during his frequent contacts with the growing child; indirectly by his advice to the parents, particularly in relation to the prevention of emotional disturbances. To do this job effectively, he must not only know the child well, but also the total environment into which the child has inescapably entered.

In his contacts with his little patients, he must always be extremely patient, kindly, gentle and resourceful in his approach. This not only wins the confidence of child and parent, but also helps to teach the parents the art of handling children.

The mother returning home from the hospital with her new baby is beset with new and frightening experiences, not to mention inexhaustible poor advice by neighbors and fond relatives. It becomes our duty to give thoughtful and kindly consideration to all her little worries until the trivial matters

become trivial in her mind, because upon the establishment of an emotionally stable atmosphere in the home depends the prevention of most of the emotional disturbances of the young child.

Dewey, the great philosopher, has told us that "no experience is lost." Let us learn to point out to parents which are the beneficent experiences and which are the harmful ones.

Since private practitioners see only a small proportion of those needing health supervision, it should be the function of public health departments to develop a widespread program of education in mental hygiene.

This entails first educating the public health doctors, the public health nurses and social workers, the school physicians, the school nurses, the school teachers, as well as the administrative officers.

I must add one more observation, one of prime importance. Preventing emotional disturbances in children is a time-consuming job. It cannot be done *en masse*. Time enough must be allotted to determine the characteristics of each child as an individual, each one being of different constitutional calibre, and subjected to varying environmental pressures.

Illustrated Roentgenograms—A Pedagogic Aid

Louis Shattuck Baer, M.D., *San Francisco*

A PERSONAL survey has shown that, with the exception of the well-trained roentgenologist, many physicians have only a hazy conception of how to translate the heart shadow on a roentgenogram into three-dimensional meaning. Any device which will aid in a better understanding of the cardiac silhouette should be of value.

Therefore, with the aid of several standard textbooks,[1] an autopsy specimen of a normal heart, photographs of Dr. Lauri Taipale's heart model, guidance from the x-ray department,* and the helpful cooperation of the medical illustrator‡ and photographers,† the accompanying illustrations were made.

The technique consisted of making preliminary sketches on Klear Pak superimposed on the x-ray film in the proper position. After a satisfactory sketch was obtained, the permanent drawing was made with pen and india ink on the x-ray film itself. Photographs were then made of this x-ray film.

The author proposes henceforward to use the same technique in producing illustrations of any of the major cardiac abnormalities about which he may have occasion to write.

*Drs. George T. LeClercq, P. O. Sather, Wm. W. Saunders, Davin Magg.
‡Miss Kay Hyde.
†Mr. Henry Raphael and Mr. Paul Newman.

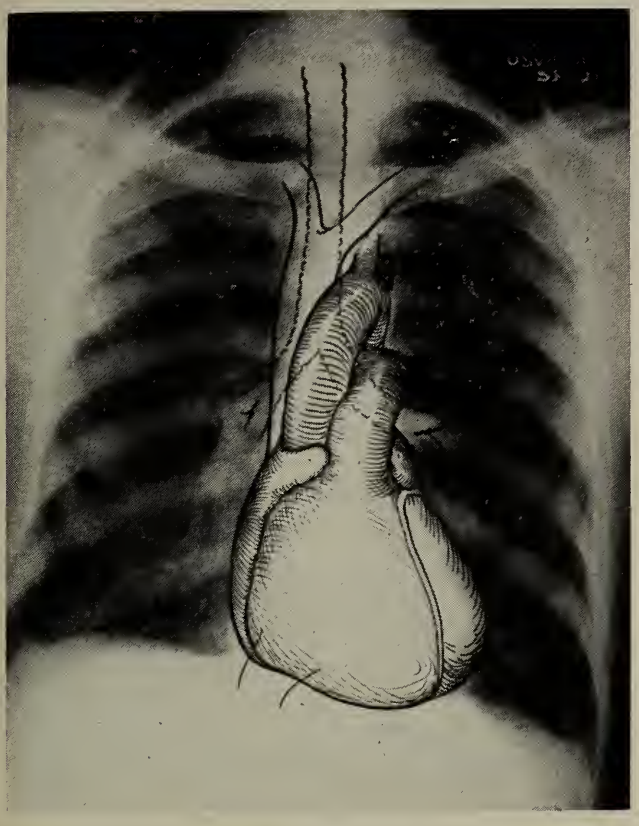
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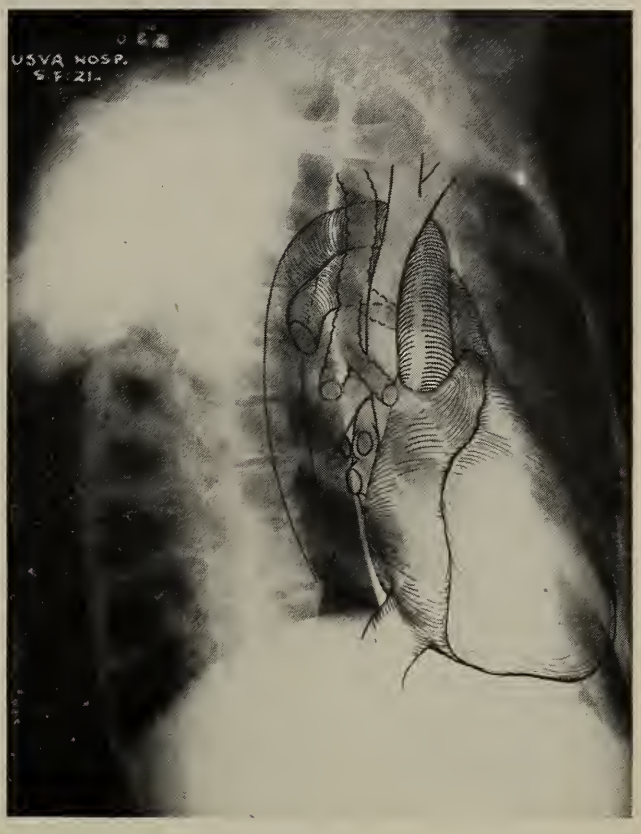
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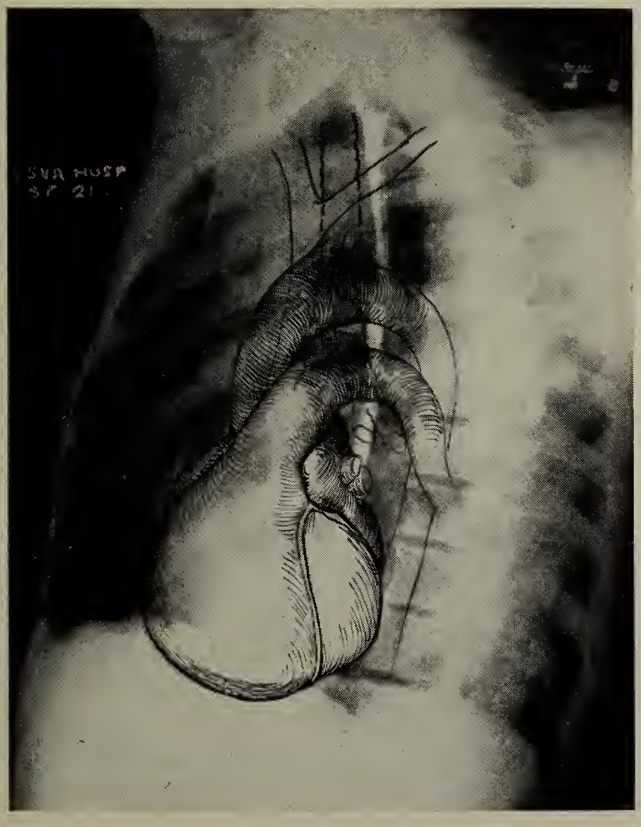
Illustrated Roentgenograms



Anterior-Posterior



Right Oblique



Left Oblique



Lateral

Prefrontal Leukotomy

Preliminary Report of 101 Cases

HARRY M. ELDER, M.D., *San Francisco,* R. B. TOLLER, M.D., *Stockton,* HARRY L. BRAMWELL, M.D., *Stockton,* and HENRY RIXFORD, M.D., *Stockton*

THIS is a preliminary report on 101 prefrontal leukotomies performed on patients at Stockton, Livermore, and San Francisco. In 90 of the cases radical leukotomies were done by trephination of the skull while the transorbital approach was used in eleven cases. This report will deal primarily with the surgical technique employed. A follow-up survey will be reported in the near future.

The patients were chosen from among the most agitated, excited and chronically psychotic, many of whom had to be kept in restraint most of the time. They were, for the most part, in poor physical condition because of the difficulty in enforced feeding and hygienic care. As this is considered a factor in the mortality rate, the rate might be expected to be lower if the operation were done on patients in better physical condition.

There have been nine deaths in the series: One from pernicious anemia six months following the operation; one from coronary occlusion on the tenth postoperative day; two from pneumonia on the 14th and 18th postoperative days; one from incision of the caudate nucleus; one from brain abscess six weeks postoperatively; one from lobar pneumonia one year postoperatively; one from edema and hemorrhage on the second postoperative day; and the ninth from spinal cord and vertebral malignancy on the eighth day following operation (this was one of the operations done to relieve intractable pain).

Many of the patients have gained from 30 to 50 pounds since leukotomy, and about 50 per cent are at present either at home or are in a condition to be taken home.

The surgical technique used by the authors differs in several respects from that used by Freeman and Watts,[1] who recently have reported a ten-year survey of the first 20 cases in which they performed leukotomy.[2]

PREOPERATIVE PREPARATIONS

The patients were given fluids, vitamins, transfusions, and any other medications which were indicated to improve their physical condition. Complete neurological and physical examinations were performed two or three days before the scheduled time of operation. An electrocardiographic tracing and a report of findings in all pertinent laboratory tests were included.

The patients were all routinely given two menadione (Vitamin K) tablets every four hours and 10 cc. of calcium gluconate intravenously once daily for two days before the operation. The morning of the operation, the scalp was shaved and cleansed with tincture of green soap, ether, and alcohol. A sterile stockinette cap was then applied. A soapsuds enema was given about three or four hours before operation to prepare for rectal anesthesia. A half hour before operation, 300,000 units of penicillin in wax and 100 mg. of demerol was given intramuscularly.

ANESTHESIA

In addition to the demerol, the patients were given avertin (50 to 65 mg. per kilo of body weight), rectally as a basal anesthesia about 10 to 15 minutes before being taken to the operating room. After the skullcap was removed and the scalp was again prepared with ether, alcohol, and tincture of zephiran hydrochloride, a local anesthetic of 1 per cent procaine was used. As most of the patients were taken to the operating room in a maniacal condition, it was often necessary to supplement the avertin and local injection with 2.5 per cent sodium pentothal intravenously.

All patients with hypotension were given 20 mg. of methedrine hypodermically. If the blood pressure dropped dangerously during the operation, the methedrine was repeated. In those cases in which more than 0.5 gm. of sodium pentothal was necessary, 1 cc. of metrazol or 1 to 2 cc. of picrotoxin was given intravenously to lessen the postoperative depression.

OPERATIVE TECHNIQUE—RADICAL FRONTAL APPROACH

After preparing the scalp, a point on the vertex, approximately 13.5 centimeters posterior to the glabella, was marked with gentian violet. The coronal suture was then palpated and two marks made on the scalp above it, one 3 centimeters to the left of the midline and the other the same distance to the right. A draped carrier (Figure 1) was placed on the forehead and the head draped.

A longitudinal incision approximately 9 centimeters in length was made on either side of the vertex through the lateral marks. The skin, galea aponeurotica, and periosteum were freed from the skull. The skull was then trephined with Cushing and McKenzie drills to the dura (Figure 2). The trephine opening was enlarged laterally with a right angle rongeur. Hemostasis was maintained by clamps, cautery, and bone wax as indicated. It was usually necessary to place small Oxycel packs between the skull and dura to control the extradural bleeding. The dura was incised along the line of the coronal suture, and two stay sutures of No. 60 cotton were placed in the edges of the incision.

Usually two or three cortical vessels were found lying just beneath the dura on the cortex. These were either cauterized or ligated with 4-0 chromic sutures on small atraumatic needles. The cortex was then cauterized at the point of cortical incision.

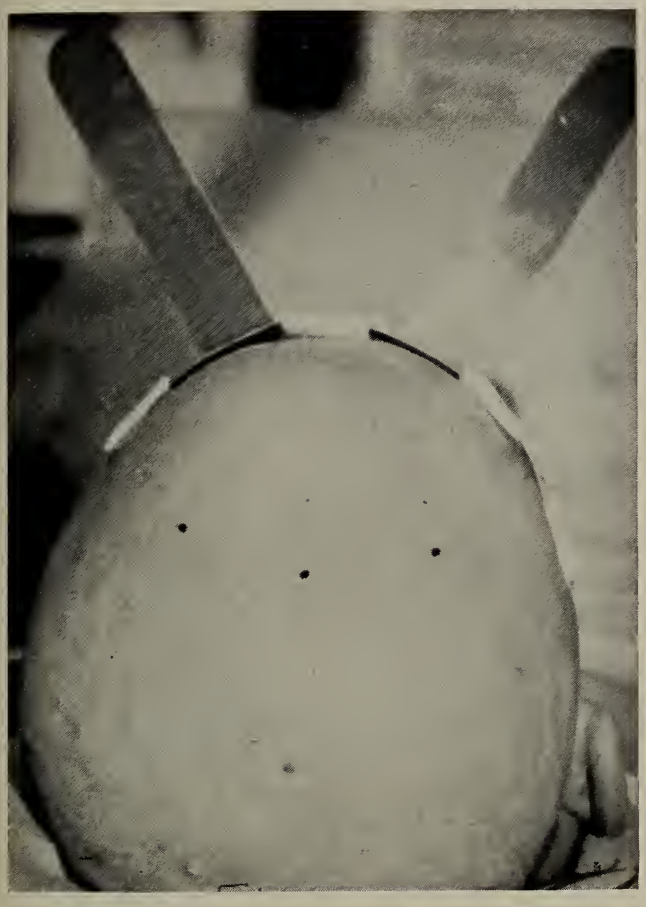


Figure 1



Figure 2

A Watts-Freeman graduated cannula then was introduced into the frontal lobe in the plane of the coronal suture. The needle was pushed downward and forward to the edge of the sphenoid ridge, which was palpated to determine the depth of the incision. If the cannula penetrated farther than 7.5 to 8 centimeters into the brain, the middle fossa had been entered. The cannula was withdrawn and pushed medially, where it was then used to probe the distance from the cortical incision to the falx cerebri. (This measurement is important in order to prevent severing the branch of the anterior cerebral artery.) The cannula was then pushed laterally to palpate for the temporal ridge. These depths were carefully noted so that the leukotome would not penetrate deeper than the white matter, especially on the medial side. (The leukotome must be kept anterior to the coronal plane during the incision of the white matter in order to avoid the caudate nucleus and other structures posterior to the frontal lobe.)

The knife-end of the leukotome, with 1-centimeter graduations (Figure 3), was inserted along the puncture tract made by the Watts-Freeman cannula. The knife blade was introduced to a distance 1 centimeter less than the distance to the sphenoid ridge (Figure 4). The white fibers of the cortico-thalamic peduncle were then severed by lateral and medial sweeps of the leukotome. During the medial sweep, the leukotome was withdrawn rapidly in order to avoid cutting the fibers in the region immediately above the olfactory tracts. (If these fibers are cut or disturbed, there is marked respiratory depression and emotional instability postoperatively. The gray matter should not be incised any more than is absolutely necessary.) The spade-end of the leukotome was then introduced through the cortical incision, and the deeper fibers were severed by a pushing motion rather than cutting. (The spade should not be pushed into the deeper medial portion of the brain above the olfactory tracts. It is very important that the incision through the prefrontal fibers lie anterior to the coronal plane. In many instances, the anterior horn of the lateral ventricle is pierced during the prefrontal incision. This is of no special importance.)

The Watts-Freeman cannula was then introduced into the wound and the stylette removed, following which a 2 cc. syringe was placed on the end of the cannula and the brain washed with two or three syringes full of saline. (The returning fluid should be blood-tinged for a few minutes. Usually, not more than 3 to 5 cc. of blood is washed from the wound.) In two or three cases, it was necessary to introduce fiberfoam into the incision in order to control bleeding.

The blood pressure often dropped shortly after the incision of the second lobe. This was controlled by an additional injection of methedrine. As soon as the bleeding had been controlled, the wound in the dura was closed and the scalp wound closed with No. 30 cotton sutures. Sutures in the scalp were removed after 12 to 14 days.



Figure 3



Figure 4

OPERATIVE TECHNIQUE—TRANSORBITAL APPROACH

Transorbital leukotomies were used on the milder patients and on patients under 40 years of age.

The patient was placed on the operating table, and intravenous sodium pentothal was given. The face and eyelids were then prepared with soap and water and aqueous merthiolate. Two drops of penicillin G solution (100,000 units per cc.) was placed in each eye.

The upper eyelid was raised and the transorbital leukotome introduced into the palpebral sac and forced against the supra-orbital plate, the leukotome being kept parallel to the bridge of the nose. When the highest point of the dome of the supra-orbital plate was palpated, the leukotome was driven into the frontal lobe of the brain, a distance of about 5 centimeters.

The fibers of the frontal lobe were severed by lateral and medial sweeps of the leukotome. (During this maneuver, care must be exercised to keep the leukotome parallel to and in the plane of the bridge of the nose.) The leukotome was then removed and pressure bandages placed over the eyes.

There was usually very little agitation or pain following this procedure. However, 10 mg. of morphine was given if the patient complained of headache or was disturbed. Occasionally, sedatives were necessary for 10 to 12 hours.

Our experience with the results of the transorbital leukotomies has been rather disappointing because of the duration of the patients' symptoms. Of the 11 patients in whom transorbital leukotomy was done, eight are to be re-operated upon, using the radical technique.

POSTOPERATIVE CARE

Immediately following the operation, light casts were applied from the wrist to the mid-portion of the upper arm. This greatly aided nursing care by preventing the patient from reaching the head dressings. The patient was placed in bed at approximately 15° above the horizontal. A blood pressure cuff was applied and the pressure taken every hour for the first 24 hours. If the pressure dropped below 100, the bed was lowered, and if necessary, 10 mg. of methedrine was given.

Three hundred thousand units of penicillin in wax was given each morning for three to five days depending upon the temperature reaction. If the temperature was elevated, daily leukocyte counts were made. In several cases the temperature rose but the blood count remained low. This phenomenon was accompanied by signs of meningeal irritation resembling meningismus. In these cases, the spinal canal was tapped and from 50 to 100 cc. of bloody fluid withdrawn. This was repeated daily as long as there was evidence of meningeal irritation.

The patients were usually restless for 24 to 48 hours, and during that time it was essential to keep continuous nursing service. Feeding was necessary until the casts were removed, which was done on about the seventh to tenth postoperative day. Dressings were changed as necessary. The patients were

all allowed out of bed for one-half to one hour morning and afternoon beginning the first postoperative day, with the period increased by 15 to 30 minutes daily until they remained out of bed the entire day.

Sedatives were given as indicated to patients who were unduly restless or irritable. Occasionally it was necessary to give morphine, 10 mg., hypodermically. Laxatives (milk of magnesia and cascara or other mild laxative) were given to insure proper bowel action, and enemas were given as indicated. Usually incontinent for several days following operation, the patients were taken to the lavatory every two or three hours beginning the first postoperative day. In some cases incontinence persisted for two or three weeks.

As soon as the casts were removed, the patient was taught to feed and clothe himself. This usually took four to five days. By the end of three to five weeks, the patients had made enough mental recovery to participate in the postoperative training and re-educational program.

450 Sutter Street.

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Community Health Education in Relation to The Private Physician

Martin Mills, M.D., *Richmond*

THE Richmond City Health Department has had a trained public health educator on its staff for the past 16 months. During this time, several community projects have been undertaken and at least three of these have had a direct effect on the practicing physician in the community.

The first was an immunization campaign in the fall of 1946. This was considered of first importance because of the diphtheria experience in Richmond during the preceding two years. In 1944, there were 26 cases of diphtheria and three deaths. In 1945, there were 47 cases of diphtheria and 3 deaths.

The immunization campaign was a joint project by the Richmond Citizens Health Committee and the Health Department. The Health Committee was made up of representatives from various civic and service organizations and was very active in originating and disseminating publicity regarding the campaign. Publicity methods included leaflets, posters, bus cards, newspaper articles and pictures and talks before groups. The publicity was all aimed at the parents of pre-school and first and second grade children. Our aim was not to build up imposing totals of children immunized in the free Health Department clinics alone, but to get a high percentage of infants and young children protected whether by their own physician or by the Health Department clinics. The leaflets, of which 40,000 were distributed, stressed utilization of the private physician in the immunization program. The requests were to "call your family physician" or "take your child to one of these Immunization Centers." These leaflets were distributed by Boy Scouts from door to door; through the school children of the first and second grades; through churches and Housing Authority offices; and 5,000 were dropped from an airplane with every 100th one entitling the bearer to a free ticket to a motion picture theater.

The number of immunizations done by the Health Department as a result of this campaign was not too remarkable. Completed immunizations of two injections or more for diphtheria and pertussis totaled 1,904. Of the total, 1,053 were completed against diphtheria and 851 against pertussis. Also, 472 vaccinations against smallpox were done. Many infants and children were given one injection but did not return for the second, and therefore cannot be counted as fully protected.

A significant result was that 60 per cent of the practicing physicians noticed a definite or marked increase in requests for immunization during the time of the campaign. From the statements made by physicians, it is estimated that an additional 500 or 600 children were immunized against diphtheria. Another significant result of the immunizations done by the private physicians and the Health Department is noted. In the seven months after the campaign started, we had only one case of diphtheria. In these same seven calendar months in 1944-45 there were 34 cases with two deaths; and in 1945-46, nine cases and two deaths.

Read before the sections on Public Health, General Medicine and Pediatrics at the 76th Annual Session of the California Medical Association in Los Angeles, April 30-May 3, 1947.

The second project undertaken by the Health Department was a mass chest x-ray survey of the adult population. This was made possible by the loan of a 70 mm. photofluoroscopic x-ray unit, a physician, and two x-ray technicians from the State Health Department. The actual chest survey was preceded by an intense publicity and health educational campaign, consisting of newspaper articles and pictures, posters, an overhead street banner, talks and motion pictures, and leaflets. Also, through the Richmond Citizens Health Committee, groups and organizations were contacted and special days specified for them. During January, February and March, 1947, 8,522 films were taken. Slightly over 2 per cent of the small films were read as suspicious, but when these were checked with 14x17 films, the suspect number dropped to slightly over 1 per cent. Of those cases diagnosed as tuberculosis on the basis of the large recheck film, 71 per cent were in the minimal stage of infection, 21 per cent moderately advanced, and 8 per cent far advanced.

The effect of the tuberculosis survey on the physician in private practice was threefold. As the survey started, all the physicians were invited to send any or all of their patients over 15 years of age to the survey center. Seventy per cent of the physicians took advantage of this. Some sent only a few patients, and others suggested routinely to patients that they go and have a chest x-ray. If the patient requested it, the result was sent directly to his physician; if not, a routine postal card was sent to all for whom the findings were negative. Persons whose small films were of suspicious character were visited by a staff member of the Health Department and an appointment made for taking the large film. After this was read, the patient was referred to his own physician with the film and a report or was sent to the public chest clinic at the Richmond Health Center. Of the first 109 needing clinical study, 55 went to their own physicians while 54 went to the chest clinic.

Of 17 physicians interviewed, 15 noticed a definite interest in tuberculosis among their patients. Many asked for examinations by their own physicians. One physician noted that several former patients with quiescent tuberculosis with whom he had lost touch came in for check-ups as a result of the publicity. Over half of the physicians reported that many of their patients mentioned having a chest x-ray and produced postal cards stating that they were free from lung disease. From the approval of the survey voiced by most of the physicians, one might conclude that if a small film unit always were readily available, the referral of patients for a chest film might become as routine in the general examination as a blood examination or urinalysis.

The third project was the preparation of a manual for physicians and their secretaries. This manual was designed to be used as a reference to services made available to the physician by the Health Department and to clearly define the responsibilities and duties the physician has in relation to the public health program. As stated in the foreword, "It would be desirable if physicians considered themselves ex-officio members of the Health Department in carrying out these services, since the aims of Health Departments and of the medical profession are ultimately identical."

The manual is loose-leaf, and changes may be readily made. It is divided into nine sections in the table of contents.

The first section has to do with the registration of births and deaths and instructions in the preparation of certificates so that they may conform to California law. Samples of birth, death, and stillbirth certificates are shown and all the most frequent questions in regard to these certificates are answered. Also, instructions and a sample card for registration of crippled or handicapped children are included.

The second section lists the reportable diseases in California and outlines the control measures for the commoner acute communicable diseases followed by the Health Department. When a person must be isolated or quarantined at home, our job is made much easier and more effective if the physician has already prepared the family. The special reports required for tuberculosis and venereal disease are shown and an outline is given of services offered by the Health Department for the control of these diseases, including diagnostic services, nursing follow-up, laboratory services, free drugs, and treatment facilities.

The third section enumerates those drugs and biologics available for free distribution to physicians and samples of the request forms used.

The fourth section outlines Health Department policies in regard to immunization against diphtheria, pertussis and smallpox and suggests reporting of immunizations done by physicians.

The fifth section covers the diagnostic services available in the public health laboratory; instructions for the submission of specimens, and the report forms used.

The sixth section is concerned with the maternal and child care program. A list of the child health conferences or well baby clinics is given with a summary of the services offered there. Information regarding the services available for children with rheumatic fever is also included and the method of referral of cases is outlined.

Other health agencies in Richmond are described in the seventh section. These include the Isolation Hospital, Richmond Health Center, Red Cross Visiting Nursing Service, Emergency Hospital, Planned Parenthood Clinic, and the National Foundation for Infantile Paralysis. Other agencies to be included at the first revision of the manual will be School Health Services, Tuberculosis and Health Association, Crippled Children Society, and the Welfare Department.

The eighth section summarizes the physicians' public health services and Health Department Services to the medical profession and the city.

The last section is a condensed summary of certain California Public Health laws, including those relating to venereal disease, prenatal examinations, communicable disease, and vital statistics.

When this manual was ready, it was presented personally to each Richmond physician. At that time, the physician was invited to allow his secretary to attend a meeting at which the contents of the manual were discussed in some detail. Approximately 15 secretaries attended the meeting.

It is believed this manual will prove to be a convenience to the physician. For the established physician, it will serve as a refresher or reminder of things already known; for the newly settled physician, it will be a complete guide to the public health program; and to both physicians and the Health Department, it will be a statement of the close relationship between them.

CONCLUSION

1. Health education and publicity have a measurable effect on the private practice of medicine.
2. This demonstrated effect is to the advantage of both the private practitioner and the Health Department in that the aims of both are furthered and the services that both offer are more intelligently used by the public.
3. Many people will be spurred to action by a newspaper article or leaflet but will go to their own physician rather than to the Health Department for services.
4. One of the means of defining and clarifying the close relationship between the Health Department and the private physician is the preparation of a manual outlining their mutual services and responsibilities.

Richmond City Hall.

Discussion by L. H. Fraser, M.D., *Richmond*

Since the inception of the modern movement of compulsory health insurance, both national and local, one hears and more often reads that medicine as a private enterprise is at the crossroads.

The arguments in favor of this compulsory health program are intended to be an indictment against our public health system now in existence as well as the private practitioner, whether general or specialist, in their failure to provide adequate medical care for the population at large.

In the words of Dr. Mills, as stated in the foreword of his manual "The aims of health departments and of the medical profession ultimately are identical," this means that community health education in relation to the private physician is also reversible in that the cooperation of the private physician with the community health program is absolutely essential for the betterment of the health of the community.

The health department, whether city or state, is tax supported and consequently comes under the scrutiny of taxpayers' associations and the governmental agency which employs it, whether state, county or city.

City councils and county supervisors unfortunately measure the public health value to their constituents in dollars and cents. The scramble for providing ways and means of raising more revenue for the support of most of the communities in California endangers the appropriations for public health programs. In Richmond the cost of our health department represents less than fifty cents per capita; yet the public health department item sometimes looms large in the eyes of politicians and public spirited lay citizens who are appointed by them to study budgets and devise methods of raising money to meet them.

It is therefore essential that a community health program be worth to the taxpayer the money that he is investing in it. To this end it is absolutely essential that the private physician strive to give such a program in his community his wholehearted cooperation. I think we all agree that the well-organized and well-administered community health program under the direction of an able health officer can do much to improve the lot of a private physician, as demonstrated by Dr. Mills in Richmond. I wish to stress, however, how much more valuable to the individual citizen of a community would this service be if the individual physician's cooperation were improved. Health officers in our inflated wartime communities such as Vallejo, Richmond and San Diego have done a wonderful public health job. I think their records speak for themselves. If the fine work of these health officers and others throughout the state is to maintain its past and present standard, cooperation from the individual physician will have to be greatly improved.

The various services enumerated by Dr. Mills in his manual are available free of charge to our patients. These include laboratory procedures, material for immunization, arsenicals, plasma and even consultation with the health officer in questionable contagious cases. Every physician in a community where such services are offered by the health department should make them available to his own patients and thereby help lighten their financial medical burden.

The local health department, while a public agency, is still administered by a member of private medicine, and whatever its success or failure in a community, it will reflect on the profession as a whole. The public health department is an efficient advertising medium of private medicine to the public and will remain such an instrument only if it is kept under control of private medical enterprise and its official bodies. To this end, cooperation of all the practicing physicians, whether general or specialist in a community, is absolutely essential.

In Richmond, the value of our own health department, under the able direction of Dr. Mills, has been well exemplified to the public. A large measure of this success has been due to the wholehearted support of the local profession. Dr. Mills has been most kind in sharing the credit for the fine work that he has done in Richmond with his colleagues in local practice. This, I believe, is a healthy attitude which goes a long way toward convincing the public that the present system of medicine, whether private or public, is still the American way.

I wish to congratulate Dr. Mills for this fine contribution, and urge members of this association to utilize to the fullest extent the facilities of their local health department.

CASE REPORTS

◀ Intracranial Metastases of Primary Pulmonary Carcinoma: A Diagnostic Difficulty

◀ Friedlander Bacillus Meningitis

Intracranial Metastases of Primary Pulmonary Carcinoma: A Diagnostic Difficulty

MICHAEL B. SHIMKIN, M.D., *San Francisco*

ERRORS in clinical diagnosis are most often referable to the fact that the particular disease of the patient is not considered by the clinician. Secondly, errors are sometimes made because certain conditions simulate each other and the secondary effects overshadow the real nature of the illness. It is inevitable that clinical errors usually are most apparent in retrospect and that the true extent of the difficulties during the course of the patient's illness is obscured by the definitive findings at necropsy.

The difficulties in the differential diagnosis between primary intracranial neoplasms and secondary intracranial growths, particularly in bronchogenic carcinoma, are well recognized. Carcinoma of the lung metastasizes to the brain more frequently than neoplasms of other portions of the body. Necropsy material reveals intracranial metastases in 15 to 30 per cent of cases of pulmonary carcinoma;[6,8,14] metastases to the brain in other forms of cancer occur in about 1 per cent of the cases.[6] Of metastatic brain tumors, approximately 50 per cent have the primary source in the lung.[10] Bronchogenic cancer probably reaches the central nervous system by way of the blood stream. Cell emboli from pulmonary tumors may thus pass from the pulmonary vein and heart directly into the general and the cerebral circulation, whereas similar emboli from elsewhere in the body on their way to the central nervous system have to pass through the pulmonary circulation and are retained in the sieve of the pulmonary capillaries.

Clinically, 60 to 70 per cent of patients with bronchogenic carcinoma have symptoms suggesting pulmonary disease.[9,14] The clinical picture in about 10 per cent of the cases is that of an intracranial lesion.[1,15] The problem of differentiating primary brain tumors and brain tumors metastatic from primary pulmonary carcinoma is encountered approximately 1700 times each year in the United States, considering that some 175,000 people die of cancer annually, and that about 10 per cent of these have cancer of the lung.[15] A report on 448 cases of pulmonary cancer at the Mayo Clinic[16] states that 52, or 12 per cent of the patients, had symptoms referable to the central nervous system. In 19 cases the initial and predominant symptoms were those of brain involvement, and in eight cases a localized brain lesion was suspected; two patients underwent exploratory craniotomy.

The difficulties that are encountered in some of these cases[4,8,10,13,16] are well illustrated in the reports of two patients observed at the Tumor Clinic, Marine Hospital, Baltimore*. Even a cranial operation did not clarify the diagnoses in these cases, and the records would have shown them as brain tumors if necropsy had not been performed.

Director, Laboratory of Experimental Oncology, University of California Medical School, San Francisco, and the National Cancer Institute, National Institute of Health, United States Public Health Service.

*Dr. John E. Wirth, director, to whom the author is indebted for permission to report the cases.

CASE 1

A 54-year-old Norwegian longshoreman was admitted to the hospital with the chief complaint of recurrent convulsive seizures.

Present Illness: Thirteen months before admission, the patient had had a convulsive attack, during sleep, characterized by loud grunting respirations, foaming at the mouth, turning of the head to the right, and spasmodic movements of the extremities. He had had six similar nocturnal seizures at monthly intervals. About 20 minutes before the attacks the patient had marked generalized headache. The convulsions, sometimes accompanied by vomiting of a projectile type, and more recently by incontinence of urine and feces, lasted a few minutes and were followed by a period of unconsciousness lasting up to three hours. After the attacks there were persistent headache and backache, which were accentuated by stooping. The convulsions gradually became more frequent and marked and occurred during the day as well as at night. Progressive dimness of vision developed in the left eye, with loss of memory, general deterioration, and loss of strength.

Past History: The patient's mother and three siblings died of pulmonary tuberculosis. The patient had had a cough with whitish sputum for the past three weeks but denied other pulmonary symptoms. During the past year he had gained 65 pounds over his normal weight of 185 pounds.

Physical Examination: The patient was well-developed, obese, and did not appear ill. The temperature, pulse, and respirations were normal. The vision in the left eye was destroyed except for an island through which only form could be distinguished, above and to the right of the macula in the field. There were bilateral retinochoroiditis and incipient cataracts; there was no papilledema. The lungs were normal except for harsh breath sounds and occasional dry rales over the right apex posteriorly. The heart was normal; the blood pressure was 150 mm. systolic and 88 mm. diastolic. The abdomen, genitalia, and the extremities were normal. Result of examination of the nerve system was essentially negative.

Laboratory Findings: The blood and the urine were normal. Results of the Kline and Eagle tests were negative. Spinal puncture showed the fluid to be under a pressure of 320 mm. of water. The fluid was xanthochromic, contained 107 mg. per cent of protein, and was slightly turbid. Pandy test showed 4 plus. Kahn test was negative, and the gold curve was 11111. Another spinal puncture done ten days later showed the fluid to be under a pressure of 250 mm. water. The fluid was clear with negative Kahn and Eagle tests, a flat gold curve, and no increase in globulin.

A roentgenogram of the chest showed a mottled infiltration throughout both lungs, the greatest change radiating laterally to the right lung root area. These changes were reported as strongly indicating a tuberculous infection.

A ventriculogram showed air in both lateral ventricles. Both ventricles of the brain were slightly enlarged, and there was a prominence seen in the upper wall of the left ventricle which projected downward. An encephalogram also demonstrated this defect. An electroencephalogram study indicated

that a space-occupying process in the left frontal region was likely.

Course: The patient had a convulsion two weeks after entry. It began with loss of consciousness and deep respirations, followed by tenseness of the body and slight clonus. Both arms were rigidly fixed and jerky, and there was carpopedal spasm. The eyes were turned to the right and the pupils were widely dilated. The patient voided involuntarily.

The convulsion, during which the patient became cyanotic, lasted about three minutes. However the patient was not able to respond to questioning until a half-hour later.

Craniotomy was performed six weeks after entry. When the dura was opened the cortex was pale and there was slight increase in intracranial pressure. A needle introduced into the superior frontal gyrus to a depth of 1 cm. entered a cavity which contained a large amount of liquefied blood. The cavity was evacuated after incision and washed out with saline.

Histologic examination of a small bit of tissue removed at operation showed it to be a piece of cortex in which was embedded a piece of tissue composed of papillary epithelium lined by tall, columnar cells with suggestion of mucus formation (Figure 1). It was felt that this was probably a metastatic papillary carcinoma, possibly from the lung. After considerable study, however, this impression was changed to a papilloma of the choroid plexus, similar to the cases described by Van Wagenen.[17] Consultation with an authority on this type of neoplasm produced the following statement: "The tumor is a perfectly benign growth of the choroid plexus and represents in all probability a fragment of papilloma. There is no question in my mind that it is not a pulmonary carcinoma."

A month after operation the patient had another convulsion, and an attempt to remove the brain tumor was made. It was found that the cyst had not recurred. In its place there was definite solid tumor tissue, which was exposed and was found to extend backward under the motor cortex. A considerable amount of the tumor was removed. Histologic examination of the mass revealed an appearance seen previously. Diagnosis of papilloma of the choroid plexus was reiterated.

The patient recovered from the operation and was discharged. However, he continued to have convulsive seizures and gradually became more somnolent, apathetic, and deteriorated. Roentgen therapy over the head was started in an attempt to alleviate the convulsive seizures. Under this therapy and phenobarbital, the patient's condition appeared to become quiescent. Repeated roentgenograms of the chest showed slow, slight increase in the density of the numerous areas of infiltration seen previously. One area extending laterally from the right lung root shadow was approximately 3x5 cm. in size (Figure 2). The patient's course continued slowly downhill. He died following a convulsion from which he did not recover consciousness, 13 months after his initial entry to the hospital and 26 months after his initial convulsive seizure.

Clinical Impression: Papilloma of choroid plexus. Pneumoconiosis or tuberculosis of lungs.

Necropsy: The ventricles of the brain were dilated, and the corpus callosum was markedly thinned. There was no tumor in either of the lateral ventricles, and the choroid plexus appeared normal. The left hemisphere, at a section passing through the genu of the corpus callosum, showed a major defect 4 cm. in diameter, communicating with the cortex superiorly and opening into the anterior pole of the left lateral ventricle. The walls of this cystic cavity were irregular in contour, granular, and yellowish. There were solid nodular areas in the grey matter of the insula, and in the grey matter of the parietal lobe near the sagittal sulcus. Similar tumor areas 1 to 5 cm. in diameter were also encountered in the nucleus ruber, the parietal occipital region, and the superior portion of the occipital lobe. The right hemisphere of the brain had a large cystic cavity 5 cm. in diameter occupying most of the frontal lobe. It communicated with the right lateral ventricle. There were numerous small areas of tumor in the cortex of the right hemisphere in a section passing through the optic chiasm, and in the cortex from here to the occipital end of the brain. In the white matter of the occipital pole was a nodule 2 cm. in diameter.

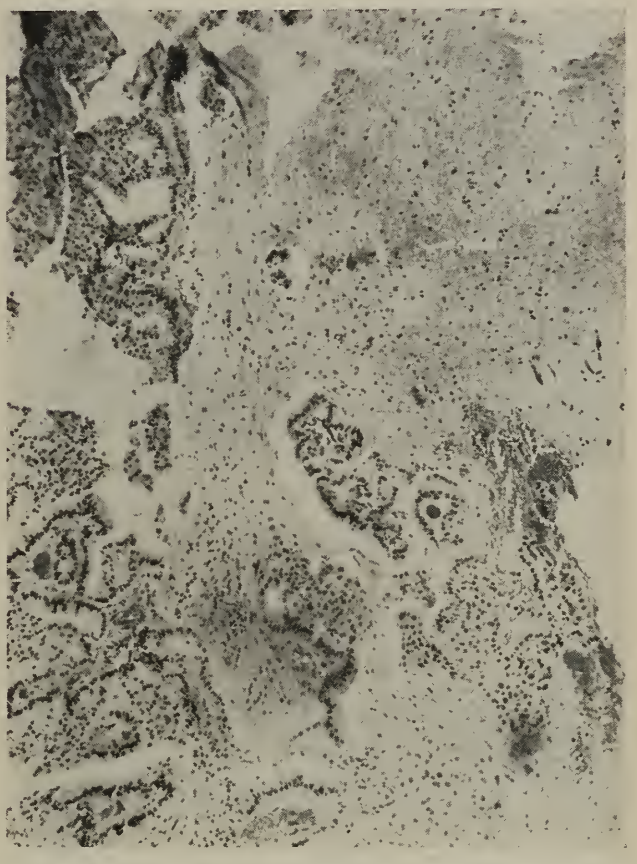


Figure 1.—Case 1 (M. J.). Section of tumor removed from the brain, showing a papillary growth that was mistaken for a papilloma of the choroid plexus. Haematoxylin and eosin (x 150).

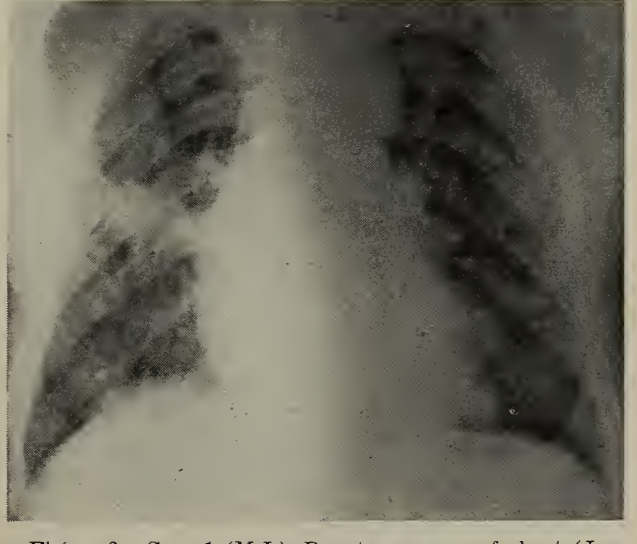


Figure 2.—Case 1 (M.J.). Roentgenogram of chest (January 2, 1942), showing diffuse mottled infiltrations throughout both lungs and a density extending from the right lung root.

The left pleural cavity was free of adhesions, but over the surfaces of the parietal pleurae there were small, firm, white nodules attached to the pleural surfaces. These nodules were up to 5 mm. in diameter and were arranged linearly along the intercostal spaces. The right pleural cavity was adherent over its total surface, and in the superior mediastinum there was a large fibrous mass, 5 cm. in diameter, which was attached on one side to the pericardium and on the other to the hilar surface of the right lung. The mass was firm and showed small areas of calcification. There were a few scattered calcified areas in the neighborhood of the mass in the lung tissue.

Both lungs showed firm nodules scattered irregularly throughout the upper and lower lobes. On cut section these were well-circumscribed, rubbery areas, 1 to 2 cm. in diameter, which were not associated with the bronchi.

Microscopic examination of the choroid plexus revealed a perfectly normal structure covered by a single layer of uniform cuboidal cells with eosinophilic cytoplasm. There was some superficial resemblance between the choroid plexus and the papillary projection seen in this tumor, in that the cells of the tumor were cuboidal, showed a regular single cell layer and eosinophilic cytoplasm. In some areas, however, the epithelium of the tumor showed a tendency to produce mucin and form granules. In one of the small brain metastases, the tumor was much more solid and in some areas appeared to be an epidermoid carcinoma.

Microscopic examination of the white nodules in the left pleural cavity revealed that the major portion of these nodules was composed of a dense collagenous tissue. At the base of this connective tissue, however, there was evidence of tumor in the form of alveoli and glandlike arrangements. The nodules in the lung were also composed of tumor, of the same papillary type but more tightly packed. In addition, there were areas of the lung in which solid masses of tumor were present within the alveoli and showed the pavementlike arrangement of epidermoid carcinoma (Figure 3).

Metastases of the tumor were present in the hilar lymph nodes, the liver, and the kidneys.

Final Diagnosis: Carcinoma of the lung with metastases to the pleura, liver, kidneys, lymph nodes, and brain.

COMMENT

The symptoms and signs in the patient were primarily referable to the brain. The patient had a strong family history of tuberculosis. The only chest symptoms were a slight cough and production of whitish sputum for three weeks before admission. He did not produce sputum and was afebrile during the course of his illness at the hospital. The patchy, multiform areas of consolidation revealed in the roentgenograms of the chest appeared to be stationary upon repeated examinations. These facts led to the misinterpretation of the lesions as an old, quiescent, tuberculous infection.

Any possible connection between the pulmonary findings and the cranial lesion was hopelessly confounded by the erroneous histologic diagnosis of the brain tumor tissue. The first diagnosis of metastatic carcinoma was changed to papilloma of the choroid plexus and was backed by an authority on the latter type of tumors. The true nature of the process was not clarified until complete necropsy had been performed.

CASE 2

A 53-year-old white marine engineer was admitted to the hospital with the chief complaints of weakness, headaches, and progressive impairment of vision.

Present Illness: About five months previously the patient noticed that he was forgetful and that he began to have trouble with men working under him. Finally he had a



Figure 3.—Case 1 (M. J.). Primary papillary carcinoma of the lung. Haematoxylin and eosin (x 150).

"nervous breakdown." He felt dizzy, had right-sided headaches with occasional diplopia, nausea, and vomiting. His vision became progressively dimmer. He had no paralyses or paresthesias and no convulsions or periods of unconsciousness.

The condition of the patient deteriorated steadily. His wife described him as being abnormally quiet, very slow in his movements, gloomy, and negativistic. He could not remember recent events and complained of double vision and headaches. During his illness the patient had lost 40 pounds in weight, from over 200 to 160 pounds.

Past History: The patient's mother had died at age 37 of pulmonary tuberculosis, and his father at age 60 of heart disease. Three siblings were living and well. He had had no visual complaints until the present illness. About a year before admission, he was on a boat torpedoed at sea, and after being adrift for five days was rescued and taken to Africa. While there, the patient had had a protracted febrile disease, stated by the patient to have been malaria. He denied night sweats, cough, sputum, or hemoptysis.

Physical Examination: The patient was well developed, fairly well nourished, and appeared to be chronically ill. The temperature, pulse, and respirations were normal. The skin had many dry scales and pigmented nevi characteristic of ichthyosis.

The patient was able to distinguish fingers at 20 feet. There was right hemianopsia of both eyes and a convergence paralysis. There was paresis of the left medial and right superior recti. Papilledema was present on the left side. The tongue protruded to the right, and a slight tremor was present. The chest was normal to inspection, percussion, and auscultation, as were the heart and the abdomen. Blood pressure was 130/88. Rectal examination revealed a slightly enlarged prostate.

Examination of the nervous system showed that the right side of the face and body were weaker than the left. The gait was unsteady, and Romberg's sign was present, with the falling to the right. The deep reflexes on the right were diminished. Right abdominal and cremasteric reflexes were not obtained, and there was a Babinsky reflex on the right side. The position sense of the right leg and foot was impaired.

The speech was slow and halting; the patient forgot complete sentences, and his immediate memory was poor. He was oriented to time and place.

Laboratory Findings: The urine and the blood were normal, the results of Kline and Eagle tests negative.

A roentgenogram of the chest showed an area of density without any borders, which extended upward from the right lung root and involved the lower medium half of the upper right lobe. No changes were seen above the shadow of the clavicle, and the margins faded out gradually (Figure 4). The findings were interpreted to indicate the presence of moderately advanced pulmonary tuberculosis.

An encephalogram showed a large defect in the region of the left lateral ventricle which deformed both the upper and lower sections of this ventricle and also displaced it to the right side. There was also some displacement of the right lateral ventricle.

Clinical Impression: Malignant brain tumor of left temporal-parietal region. Pulmonary tuberculosis of right upper lobe.

Course: The patient underwent craniotomy one week after entry. The brain was under marked tension, and there was some herniation of the cortex when the dura was opened. Several centimeters below the cortex a large infiltrating tumor was encountered, extending deep into the midline. A large portion of the infiltrating mass was removed.

Pathologic examination of a number of sections taken from various portions of the tissue showed a large amount of tissue which was uniform in structure and appeared to be composed chiefly of fibroglia fibers with a rather even distribution of astrocytes. The tissue contained moderate-sized areas of hemorrhage and small areas of calcification; there were also small areas of inflammation. The diagnosis of fibrous astrocytoma was reported.

The patient recovered from operative shock, but his general condition remained poor. He was aphasic and had complete paralysis of the right arm. Three days post-operatively he developed an area of consolidation at the left lung base and expired in coma two days later, about six months after the onset of the initial symptoms.

Necropsy: Significant findings were limited to the head and thorax. The skull was considerably thinned out, more so on the left than on the right, and in the temporal region in some places was about 1 mm. in thickness. There was a large hemorrhagic and necrotic process involving an area of about 8 cm. in diameter in the left temporal and parietal region. The vessels at the base of the brain, the pituitary gland, and the dural sinuses were normal.

The right pleural cavity showed old fibrous adhesions over the apex; the left pleural cavity was free of adhesions. The posterior and inferior portions of both lungs revealed nodular consolidation and large amounts of fluid and blood, and small amounts of purulent material were expressed from the cut sections of these areas. In the apex of the right lung there was a gelatinous consolidation studded with chalky white areas. In conjunction with this process was an old area of cavitation about 2 cm. in diameter.

Microscopic examination of the large hemorrhagic, necrotic mass in the brain revealed no evidence of glioma. There were numerous areas in which the brain tissue was markedly changed, and there were areas of gliosis, which undoubtedly led to the erroneous diagnosis of astrocytoma. In the most posterior portion of the hemorrhagic area, there was a large tumor nodule composed of necrotic, metastatic carcinoma. The area was at least 3 cm. in diameter.

Microscopic examination of the nodular areas in the apex of the right lung revealed nests of tumor cells which had abundant eosinophilic cytoplasm with sharply marked cytoplasmic boundaries. In some areas the nests of cells were arranged in a pavementlike pattern. Between these nests of



Figure 4.—Case 2 (J. C. B.). Roentgenogram of chest (December 6, 1941), showing a density without borders in the right upper lobe, extending upward from the right lung root.

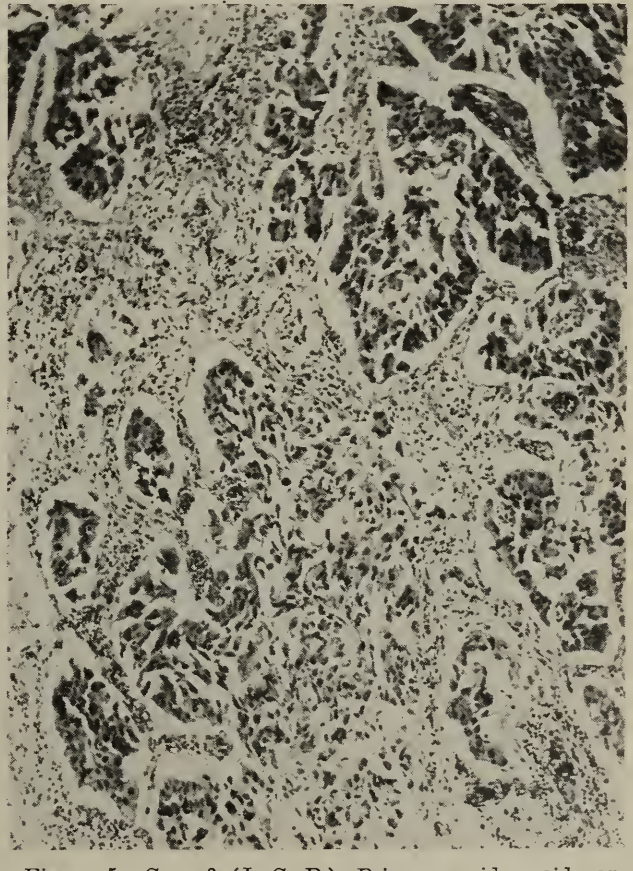


Figure 5.—Case 2 (J. C. B.). Primary epidermoid carcinoma of the lung. Haematoxylin and eosin (x 150).

cells there was a considerable degree of fibrosis, and the areas as a whole were walled off by a heavier wall of fibrous connective tissue (Figure 5). There was widespread confluent bronchopneumonia. There was no evidence of tuberculous infection.

Final Diagnosis: Epidermoid carcinoma of the right lung, with metastasis to the left cerebral hemisphere; terminal bronchopneumonia.

COMMENT

The symptoms and signs in this case were limited to the brain. The patient had a family history of tuberculosis, but otherwise no indication of a pulmonary lesion was present until the roentgenogram of the chest was obtained. It was felt in retrospect that the roentgenogram should have led to a greater consideration of a primary pulmonary carcinoma, since it revealed a unilateral density near the hilus ramifying into the parenchyma in a man of 53, whose clinical course was afebrile and without other evidence of pulmonary tuberculosis.

The chief confusion, however, arose because the glial reaction of the cerebral tissue was interpreted as caused by an astrocytoma, rather than by metastatic carcinoma. Such reactions to metastatic lesions are encountered frequently, the response being much like that found in wounds and infections of the brain.[8] As in the first case, this led to the erroneous clinical and gross pathological diagnosis and a discounting of the pulmonary process—errors that were not rectified until the microscopic examination of the tissues at necropsy.

DISCUSSION

The clinical diagnosis of primary pulmonary carcinoma in a patient with symptoms and signs of a brain lesion is based upon suspicion and upon verification of the suspicion. Fried and Buckley[8] believe "that when a person of middle age has an abrupt onset of symptoms and signs of a rapidly developing intracranial lesion, a metastatic cerebral lesion should be thought of, and that the lungs are the most common site of the primary lesion."

The age and the mode of onset of symptoms, however, are not clear indications. About 10 per cent of bronchogenic carcinomas occur in individuals under 40 years of age,[14] and the onset of cerebral symptoms may be quite gradual. It is apparent that it should be a routine procedure to obtain roentgenograms of the chest, as well as to attempt to rule out other neoplastic foci, in all patients suspected of having a primary neoplasm of the central nervous system.

The symptoms, signs, structure of tissue, and other features of primary carcinoma of the lung have been the subject of numerous excellent papers and monographs and need no reiteration here. In the 10 per cent of cases in which the presenting symptoms of the disease are those of intracranial disturbance, roentgenograms of the chest are usually the first and the chief diagnostic aid. The roentgenographic features of pulmonary carcinoma vary greatly, and roentgen examination does not establish a definite differential diagnosis even in extensive involvements,[2] but the roentgenogram does show the presence of a lesion in over 95 per cent of the cases.[18]

The presence of a lesion in the lungs of a patient with manifestations of an intracranial process should indicate a further and exhaustive investigation of the intrathoracic findings.

Further roentgenographic studies, such as exposures from several angles, and fluoroscopy, are useful particularly in the case of lesions at the root of the lung. Special techniques, particularly bronchography with the aid of iodized oil,[7] and tomography,[20] are often valuable. Demarcation of peripheral masses may be facilitated by roentgenograms following artificial pneumothorax.

Examination of the sputum or of pleural exudate may reveal the diagnosis by the demonstration of neoplastic cells. Wandall[19] found cells of malignant tumors in the sputum of 84 of 100 patients with bronchogenic carcinoma, and Herbut and Clerf made the finding in 22 of 30 such patients. The presence of tubercle bacilli does not rule out carcinoma, as Brunn[3] reported this organism in 10 per cent of 626 patients who had pulmonary carcinoma.

The bronchoscope is an invaluable instrument in the examination of the respiratory tract. Jackson[12] stated that bronchoscopic examination and biopsy will establish the diagnosis in about 75 per cent of the cases. Direct aspiration biopsy may be helpful in peripheral lesions not accessible to the bronchoscope.[5]

It has been stated[4, 8] that when a single tumor in the brain is the only demonstrable metastasis and the primary pulmonary carcinoma is slowly growing, enucleation of the cerebral lesion has led to prolongation of the patient's life and to relief of suffering caused by the expanding intracranial lesion. At least the prolongation of survival has been questioned;[16] the length of life of these patients is approximately six months after onset of symptoms.

SUMMARY

The diagnostic problem of differentiating intracranial metastases of primary pulmonary carcinoma and primary intracranial neoplasms is illustrated by a review of two cases.

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Friedlander Bacillus Meningitis

Bernard Hyde, M.D., and Leroy Hyde, M.D., *Los Angeles*

FRIEDLANDER bacillus meningitis is rare. Thirty-three cases have been reported in the literature.[4, 6, 8, 9] In a recent report, Pain and his co-workers[7] note a case of Friedlander bacillus, type A, meningitis, with the organism secured from cerebrospinal fluid, blood and aural discharge. The patient received sulfadiazine, penicillin, and streptomycin, but died 33 hours after the first dose of streptomycin. In almost all cases there has been coincidental septicemia, and almost all the patients have died. The disease was found to originate in the lung in five of 29 cases reviewed by Ransmeier.[8] In 1943, 51 cases of primary Friedlander bacillus pneumonia were reported,[5] and among them were two cases of Friedlander bacillus meningitis secondary to Friedlander pneumonia.

CASE REPORTS

Case 1. The patient (Case 9 of the Friedlander pneumonia series)[5] was a 52 year old white male. He entered the hospital in a preterminal comatose state, and died in seven hours. Friedlander bacilli, type A, were cultured from the sputum, blood, and cerebrospinal fluid. The patient had pneumonia involving the right upper lobe and the left lower lobe, and also meningitis. He died without receiving any specific therapy. (Pre-chemotherapy era.) At autopsy, pneumonia and purulent meningitis were the chief findings. Postmortem cultures of the lung, meninges, and spleen were positive for Friedlander bacilli, type A.

Case 2. The patient (Case 50 of the Friedlander pneumonia series)[5] was a 37 year old white male. He entered the hospital acutely ill, with cough and thick, tenacious, mucopurulent, blood streaked sputum. Examination and a chest roentgenogram revealed pneumonia of the entire left lung and, in addition, signs of meningitis were present. Friedlander bacilli were cultured from the sputum, blood and cerebrospinal fluid. No typing of the organism was done. The patient died on the fourth hospital day after an acute toxic course. No chemotherapeutic or anti-biotic agents were available (1935). Postmortem examination revealed a Friedlander pneumonia and purulent meningo-encephalitis. Postmortem cultures of the heart, lung, blood, spleen and meninges were positive for Friedlander bacilli.

As in most of the reported cases of infection with Friedlander bacilli, neither of the patients received specific therapy. Two patients given sulfonamides are reported to have recovered.[8, 9] One patient treated with streptomycin died, but "the absence of gross and the nearly complete absence of microscopical evidence of meningitis at autopsy are stressed."[9] Experimental evidence indicates that both sulfadiazine[1] (Table 1) and streptomycin[2, 3] are effective in vitro against certain strains of Friedlander bacilli, although not against all.

Table 1.—*Mice Survival and Chemotherapy*

(Adapted from Feinstone, Williams, Wolff, Huntington, and Crossley[1])

	No. of Mice	Mice Surviving	Per Cent Survival
Sulfanilamide	100	2	2.0
Sulfapyridine	99	6	6.0
Sulfathiazole	100	2	2.0
Sulfadiazine	86	63	73.6
Controls	78	0	0.0

Heilman[2] studied nine strains. Four of these, type A, had not been recently isolated. Five strains had been recently isolated, but were not type A or B. All nine strains were sensitive to streptomycin in vitro, the recently isolated strains being more sensitive. Using a single strain of Friedlander bacilli sensitive to streptomycin, Heilman found that in mice inoculated intra-abdominally with 10,000 times the lethal dose of bacilli, streptomycin given three hours after the inoculation and then for a total of three days, would give complete protection. The control mice, not receiving streptomycin, were all dead within one day. Similar experiments in which mice were inoculated intra-abdominally with 1,000 times the lethal dose of a type A strain of Friedlander bacilli, and then were treated with streptomycin suspended in oil and beeswax, produced essentially similar results. When the mice were infected by intranasal doses of Friedlander bacilli type A, the protection given by streptomycin was less, although here too the drug was of definite value. The mortality rate for streptomycin-treated intranasally infected mice (seven days of therapy) was 13 per cent compared with 100 per cent for the control group. It is important to stress that streptomycin was given very soon (three hours) after the introduction of the Friedlander bacilli (Table 2). It is clear that adequate therapy had best include both sulfadiazine and streptomycin, to be given promptly and in adequate doses, and to be pursued vigorously. These drugs can be of value only before suppuration, or at least extensive suppuration, has begun. Their greatest value is, of course, at the onset of the disease. The importance of an adequate and intensive early search for bacterial invaders (smears and cultures of sputum and cerebrospinal fluid and blood cultures) is clear.

SUMMARY AND CONCLUSIONS

1. Two cases of Friedlander bacillus meningitis are reported. Both patients died, one in seven hours and one on the fourth hospital day. Sputum, blood, and cerebrospinal fluid cultures were positive for Friedlander bacilli in both cases. Neither patient received chemotherapeutic or antibiotic agents, as these were not available at the time.

2. Friedlander bacillus meningitis should be treated promptly with sulfadiazine and streptomycin, since these drugs have been shown to have value, both in vitro and in vivo.

ADDENDUM

Since this report was submitted, S. S. Jacob and F. H. Top (Annals of Internal Medicine, 28:1003-1009, May, 1948) have reported seven cases of Friedlander bacillus meningitis with two recoveries. The patients who recovered had negative blood cultures and both seemed to be helped by sulfadiazine and penicillin.

6333 Wilshire Boulevard.

From the College of Medical Evangelists, Los Angeles, and the Birmingham General Hospital, Van Nuys, California.

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TABLE 2.—*The Effect of Treatment with Streptomycin on Experimental Infections in Mice with Micro-Organisms of the Friedlander Group.* (From Heilman[2])

Infecting Dose				Treatment with Streptomycin				
Experiment	Strain	No. of Times Lethal Dose	How Given	Units per Day	No. of Days	Inoculated Mice	Mice that Died	Mortality Per Cent
1	No. 575 Type Unk.	10,000	Intra-abdominally	185	3	8	0	0
				460	2	6	0	0
				None		14	14	100
2	No. 837 Type A	1,000	Intra-abdominally	500	3	20	1	5
				250	3	20	6	30
				None		20	20	100
3	No. 838 Type A	1,000	Intra-abdominally	500	3	15	0	0
				None		15	15	100
4	No. 837 Type A	100	Intranasally	500	3	10	8	80
				None		10	10	100
5	No. 837 Type A	100	Intranasally	500	7	15	2	13
				None		15	15	100

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CORRECTION:

In an article "Inflammation as Considered by the Radiologist," by Thomas M. Fullenlove, M.D., which was published in the August issue of CALIFORNIA MEDICINE, the word "leukotoxine" as it appeared several places in the text as well as in Chart 1 should have been "leukotaxine." The author of the article explains that leukotaxine, a word coined by Valy Menkin, is a combination of leukocyte and chemotaxis. Menkin's "Dynamics of Inflammation" is cited as authority.

California Cancer Commission Studies*

Chapter XXII

Carcinoma of the Liver, Gallbladder, Extrahepatic Ducts, and Pancreas

William F. Rowe, M.D. and E. Eric Larson, M.D., *Los Angeles*

CARCINOMA arising from the liver cells or from the epithelial lining of the intrahepatic bile ducts is called primary. We designate carcinomata arising directly from the liver cells as hepatomas, and those from ductal epithelium as cholangiomas. They both occur rarely, and are quite unimportant from the surgical standpoint except when diagnosed early and confined to the left liver lobe, or when they are somewhat pedunculated. In both of these instances, surgical removal is possible. The diagnosis must be made with utmost caution and only after definite exclusion of a primary focus elsewhere in the body.

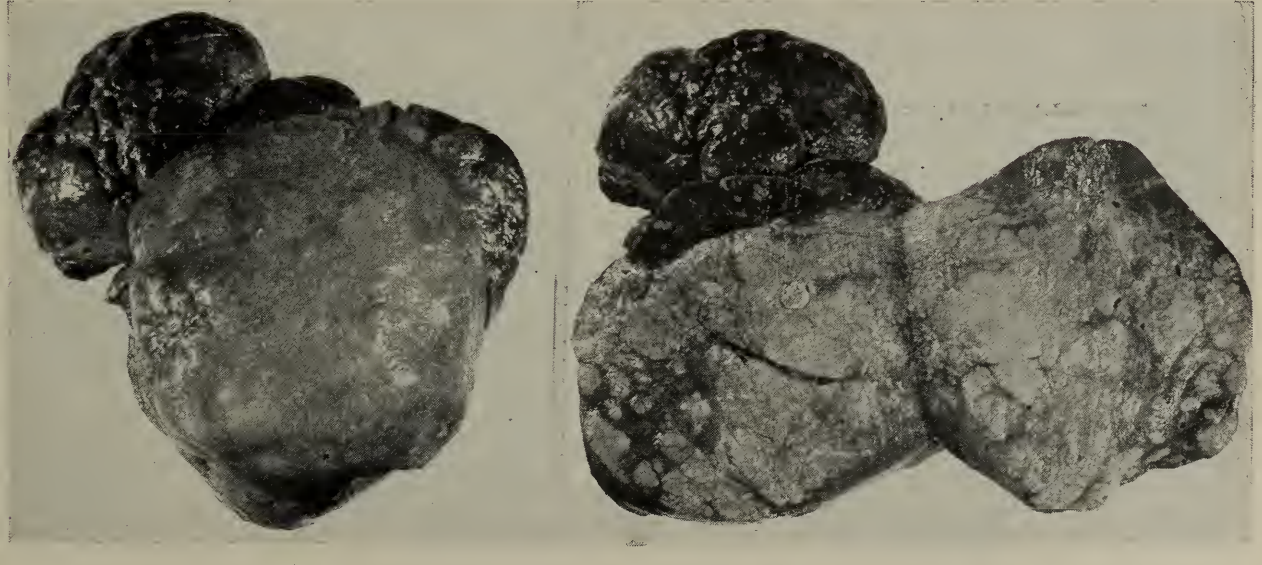
Carcinoma arising elsewhere in the body may metastasize to the liver. Such deposits are termed secondary or metastatic. The usual site of the primary lesion is in the gastro-intestinal tract, the portal drainage from which is screened by the liver. The breast, ovaries, and eye are other common primary foci that give rise to secondary liver deposits.

Advanced metastatic carcinoma in the liver is easily recognized. The liver is enlarged, having tender nodules that are readily palpated. These nodules may undergo necrosis which usually gives rise to chilly sensations in the patient, with bouts of fever. It is interesting that jaundice is usually not present in a patient with metastases in the liver, except in the terminal stages or in the occasional instance where the nodules are situated at the liver hilum and compress the main excretory bile ducts.

Lesser degrees of metastatic hepatic involvement are frequently not recognized and are difficult to diagnose. An exploratory celiotomy may become necessary. The lesion may be visualized by means of a peritoneoscope, and biopsy made. This procedure by an expert entails minimal trauma, lessened expense, and practically no pain.

The real problem is to ascertain the site of the primary growth and, in addition, to assess the confines of secondary metastatic spread. The liver is known to have great powers of regeneration and a remarkable functional reserve. This fact assumes importance since many extrahepatic primary lesions, with minimal metastatic deposits in the liver, may logically be removed. This may allow the patient to survive in comfort for quite long periods, often years. A solitary nodule confined to accessible liver areas, such as the left lobe or other superficial positions, can be removed. One thereby does all that is humanly possible for the patient.

*Organized by the Editorial Committee of the California Cancer Commission.



A B

Figure 1.—(A) Liver with pedunculated hepatoma. (B) Hepatoma sectioned. Hepatoma found in white male, aged 66, who complained of constant pain. The nodular mass was visible. No jaundice. Some ascites. Icteric index 14, serum albumin 4.9. Serum globulin 2.6. Liver function test revealed mild dysfunction. He died of bronchopneumonia. Note pedunculated fashion of growth, also portal vein filled with neoplasm.

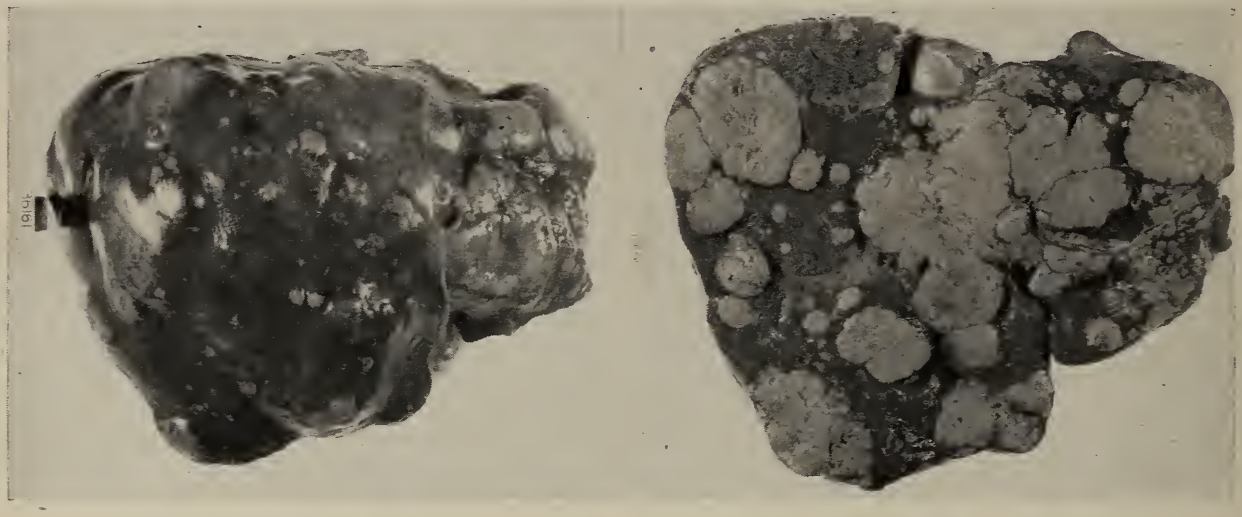
The treatment of neoplasms of the liver, to say nothing of cure, whether primary or secondary, has always been and still is a very gloomy chapter. X-ray therapy is of no value. Those who have used the Russian A.C.S. serum pronounce its use ineffective. It is to be hoped that some radioactive isotope may in time be found to be a valuable agent for this dread disease.

CARCINOMA OF THE GALLBLADDER AND EXTRAHEPATIC DUCTS

Carcinoma of the gallbladder comprises five to six per cent (Kaufmann) of intra-abdominal carcinomata and is usually associated with long-existing cholelithiasis. Due to this relationship, we find carcinoma of the gallbladder to be more frequent in females because they are more often afflicted with cholelithiasis.

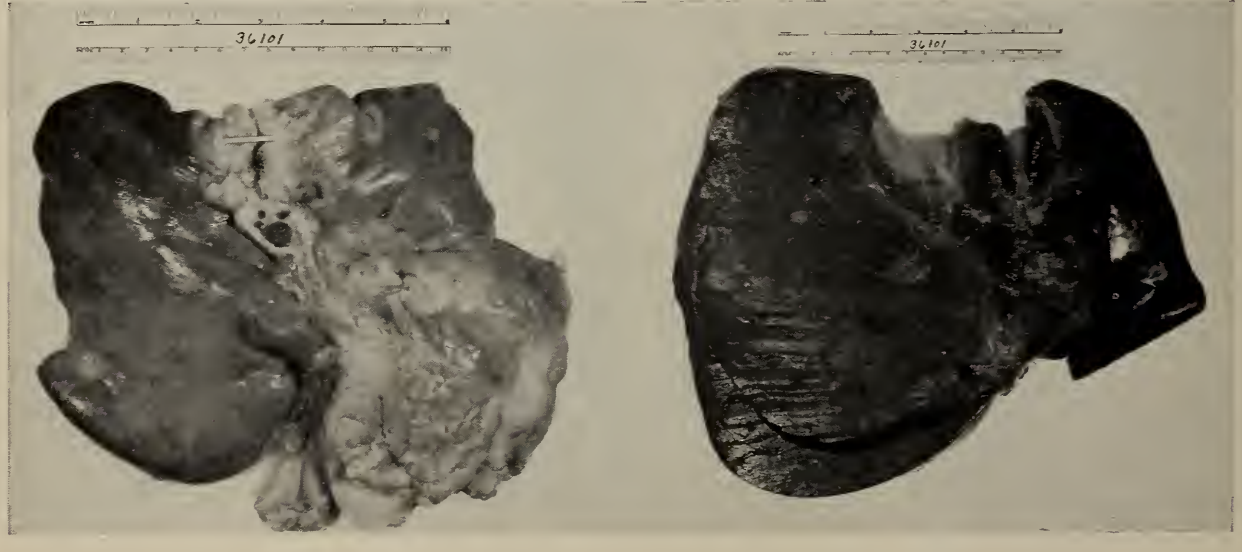
Ordinarily by the time a diagnosis of carcinoma of the gallbladder is made clinically, the lesion is already hopelessly inoperable.

The very recognition of cancer of the gallbladder is of great importance. Examination of the removed gallbladder should always be made while the abdomen is still open. A suspicious lesion requires an immediate and definite diagnosis. With the diagnosis of an early neoplasm, the surgeon should with the cautery widely remove the gallbladder bed and adjacent liver parenchyma which is always invaded early. In addition, all palpable lymph nodes along the ducts must be removed. The timid or inexperienced operator on such an occasion may do his patient grave injustice by neglecting to remove all such



A B

Figure 2.—(A) The liver containing metastatic cancer. (B) Liver sectioned. White male, aged 69, having pruritic jaundice. Liver enlarged, containing palpable tender nodules. Icteric index 130, serum albumin 4.7. Serum globulin 2.3. Prothrombin 10 per cent. Autopsy revealed a small primary prepyloric gastric neoplasm. A nodule occluded the hepatic ducts at hilum of the liver.



A B

Figure 3.—(A) This shows an opened gallbladder containing stones and extensive neoplasm. (B) The cut surface of the liver reveals widely distributed metastases. White female, aged 63. Gallbladder distress for many years. Died of endocarditis. Calculi and neoplasm of gallbladder an incidental finding.

possible invaded tissue. Hemorrhage is feared by all operators but with styptic fibrin and absorbable oxidized cellulose gauze packs, greater safety is now available in staying hemorrhage.

Prophylaxis against cancer formation in the extrahepatic system is the real responsibility of the physician. For this reason, *all patients having gall stones should be advised to have a cholecystectomy because of the possibility of cancer being initiated by the irritating calculi.* The danger of cholecystectomy with present-day methods seems much less than that of allowing a possible source of neoplasm to exist.

There are occasional instances of a primary carinoma of the cystic duct. In such instances, the whole cystic duct and adjacent lymph nodes must be removed. Obstructive jaundice may be due to a primary cancer of the common duct. It occurs rarely and its recognition at operation is important since segmental resection can be done and repair or sidetracking of the biliary flow may be made by various methods.

CARCINOMA OF THE PANCREAS

Carcinoma of the pancreas is found most commonly in males having an average age of 57 years. The neoplasm is found in the head of the pancreas in 62 per cent, in the tail in 5.5 per cent, in the body of the organ in 3.5 per cent, and diffusely throughout the pancreas in 29 per cent. The existence of the growth in the body and tail of the pancreas offers a difficult problem in early diagnosis, because there is no clear-cut symptom complex.

The symptoms of carcinoma of the pancreas vary according to the location of the lesion. A growth confined to the pancreatic head, Wirsung's duct, ampulla of Vater, or to the lower end of the common duct usually produces early obstructive jaundice. A middle aged or older person having loss of appetite, weight and strength associated with a progressively advancing jaundice, must be suspected of having a neoplasm in or near the head of the pancreas.

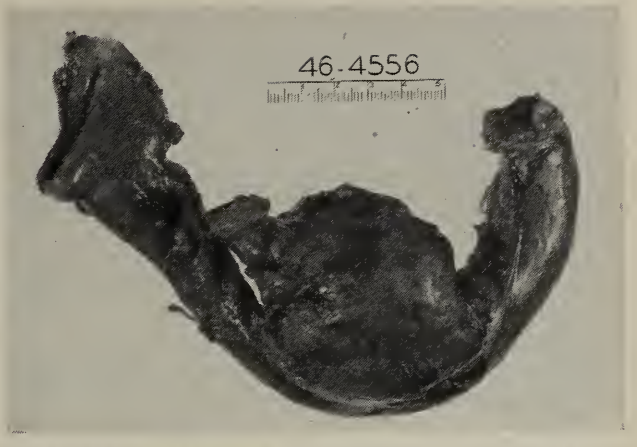


Figure 4.—This photograph illustrates by actual specimen the distorted duodenum encircling a neoplasm in the head of the pancreas.

There may be pain with the jaundice—in fact one-third of patients have associated biliary colic. Pain, though usually absent at first, may progress in severity as the growth expands, and ultimately become constant. Vomiting usually is present initially, but it is not a conspicuous symptom. Back-pressure of bile promotes a distention of the gallbladder and a diffuse enlargement of the liver. The distended gallbladder may not be palpable because of obesity of the overhanging hard tender liver edge. If it is felt, Courvoisier's law applies.

Unexplained thrombophlebitis occasionally accompanies cancer of the pancreas. Jaundice without pain is the early symptom of most concern, since it may be confused with conditions other than cancer, usually virus infection (formerly labeled "catarrhal jaundice"), or acute yellow atrophy of the liver, Weil's disease, cirrhosis, a silent common duct stone, or enlargement in or adjacent to the head of the pancreas due to inflammation.

The laboratory assists very little in establishing the diagnosis except for the estimation of the pro-



A B

Figure 5.—(A) This specimen illustrates a neoplasm at the ampulla of Vater. (B) An unsuspected, single, centrally located metastatic deposit in the liver parenchyma. White male, aged 72. Malaise seven months, weight loss 40 lbs. Icterus index 102. Prothrombin 100 per cent. Hgb. 8 gms. R.B.C. 2.5 million. Serum albumin 4. Serum globulin 1.8. N.P.N. 33. Considered an excellent case for resection of neoplasm. Modified Whipple procedure done. Died following an accident. Autopsy revealed an unsuspected occult deposit of neoplasm. Prognosis must always be guarded.

gression of the icterus, blood serum amylase activity, prothrombin level and the blood sugar level. One should try to detect whether the biliary obstruction is intra- or extrahepatic. Blood in the stool after correction of prothrombinemia is suggestive.

Roentgen studies are important since malignancy in the stomach and colon can be excluded. In addition, the x-ray may reveal the duodenum with a narrowed lumen encircled by a definite tumor.

Cholecystography is of no value since there can be no circulation of the opaque medium into the ducts or gallbladder because of the bile stasis.

Peritoneoscopy may be valuable in competent hands to detect the presence or absence of surface neoplastic deposits in the liver. Specimens for microscopy may also be taken.

TREATMENT

Diagnosis is usually shrouded in doubt and in most instances the patient should have surgical exploration. Adequate preoperative preparation of the patient, with blood, fluids, proteins, carbohydrate and vitamins including K, is essential.

The surgeon should know thoroughly the various procedures and have a full knowledge of the modern techniques which are now quite successfully used, so that he may select the procedure best suited to the circumstances as determined by a careful assay of all factors.

Infrequently the removal of a silent common duct stone will cure the patient. When the head of the pancreas is enlarged, it may be either inflammatory or neoplastic. These two conditions are quite similar and a true diagnosis can be provided only by microscopic study of specimens judiciously removed for biopsy. If the mass is inflammatory, there should be no reason for an extensive surgical procedure. The presence of a neoplasm without any extension, however, should be considered an indication for wide surgical removal. Several technical procedures in either the single or two-stage method for the removal of such a neoplasm are described in the surgical literature. The surgeon must always discuss prognosis guardedly, since occult metastases may exist.

Where inflammatory enlargement or a neoplasm beyond any hope of removal exists, the bile may be diverted by anastomosis of the gallbladder to either the stomach, the duodenum, or a loop of jejunum. Where the anastomotic operation becomes a cholecysto-jejunal fistula, it seems advisable to make an adequate anastomosis between the two limbs of the jejunal loop to prevent reflux of intestinal contents into the biliary system. This internal biliary drainage provides relief of the cholemia and the accompanying pruritis which is of great concern to the patient.

CONCLUSION

1. Carcinoma of the liver may be primary or secondary. Differential diagnosis is very important since only on very rare occasions can there be thoughts of removal of a primary lesion, while secondary deposits may be indication for surgical treatment at another site.

2. Primary cancer of the gallbladder occurs more frequently than is generally appreciated. If it is found and recognized, the gallbladder with its bed and adjacent lymph nodes should be removed, if possible. *If stones or papillomata exist, cholecystectomy is good prophylaxis against cancer.*

3. The very rare cancer of the cystic duct is often overlooked. Treatment is removal of all adjacent lymph nodes with the involved duct. Primary cancer of the common duct may be removed by segmental resection of the duct along with neighboring lymph nodes. Repair of the common duct or diversion of the bile flow can be accomplished by various proven procedures.

4. Since inflammation and tumor of the pancreas can produce the same symptoms, it is most important that biopsy be taken. Cancer in the head of the pancreas when apparently not scattered may indicate resection of the pancreatic head. This procedure entails much judgment and surgical skill.

"Cancer of the Kidney and Testicle," by Frank Hinman, M.D., Chapter XXIII of the California Cancer Commission Studies, will appear in this section in the October issue of California Medicine.

California MEDICINE

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Editor, DWIGHT L. WILBUR, M.D. *Assistant to the Editor*, ROBERT F. EDWARDS

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For Information on Preparation of Manuscript, See Advertising Page 2

EDITORIAL

Medicine in the Atomic Revolution

The atomic revolution is undoubtedly developing. No space here for a list of places where it is visible, starting perhaps with Advertising and continuing through the alphabet to (one fears) Zero Hour. Medicine is valiantly grasping at its share, or impatiently awaiting usable developments. The revolution is not coming along fast enough to please us who are so keenly aware of the many diseases we have not yet learned to prevent or cure. Particularly are we disappointed that the cancer problem is not yet solved. Cancer has already yielded a little bit to radiation (x-ray and radium). Were we too naive when we thought that surely 300 radioactive isotopes would somewhere among them produce a method of real cancer control?

Therapy with even the best proved radioisotopes (P^{32} and I^{131}) is still in the stage of clinical experiment. It may be that P^{32} will come to replace x-ray in the alleviation of leukemia (if chemotherapy doesn't get there first). And I^{131} does work to produce regression in a certain type of thyroid cancer. Its use in Graves' disease is, in the eyes of some, extremely hopeful. But nobody should at present tell the medical profession: "This is the treatment of choice; you have a duty to learn to use it." The dictum should rather be: "Patients with Graves' disease would do well to submit to this type of clinical experiment."

The Atomic Energy Commission is delivering isotopes only to those groups which have the physical and personnel set-up to make the investigations effective as research. In other words, the emphasis is on bettering medical science. The patient yields to the experiment in hope of being helped, of course, but cannot count on it.

When we look at Medicine more broadly, however—not just radioisotopes for therapy—we see that the horizon is very wide indeed. The tracer techniques, using radioisotopic labels, provide tools of amazing power for investigating the fundamental biological phenomena on which Medicine is founded. Chemists and biologists, physiologists and pharmacologists are driving lines of research out into this field in many directions. Many of the universities have one or several investigators using radioisotopes. The National Laboratories have biology divisions. Many of the researches are fundamental and it is impossible to predict which of them may yield important advances. This is true of all research, of course; one never knows where the important discoveries will appear. More and more medical schools are setting up isotope units and now the Veterans Administration is urging the creation and separate financing of such units in its hospitals.

Use in discovering the nature and causes of disease, rather than direct use in therapy, should be looked upon as the important field for isotopes. One may expect scientists to embark on more and more medical researches made hopeful of practical conclusions by the availability of these new tools (radioisotopes). Some of the researches will be at the clinical level, and in these, however much he may lean on the rest of the isotope team—physicist, chemist, and others—in these, we must realize, the doctor of medicine must be the investigating scientist.

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NOTICES AND REPORTS

State-wide Cancer Meetings Under Auspices of the Cancer Commission October 11-16, 1948

Statistics show that there were more than 14,000 deaths from cancer in the State of California during the year of 1947. Much has been done in the past few years in the way of lay and professional education, but with the constant increase in deaths, there is still a great deal to do. Regardless of the various refinements in cancer therapy, there is still nothing of so much importance as early diagnosis and institution of adequate treatment while the cancer is still in a localized stage.

With the idea of getting the latest information available on the cancer problem to physicians throughout the state, the Cancer Commission of the California Medical Association, working in conjunction with the California Department of Public Health and the California Division of the American Cancer Society, has completed plans for the first series of state-wide cancer meetings to be held the week of October 11-16, 1948.

Owing to the fact that the 34th annual meeting of the Clinical Congress of the American College of Surgeons will be held in Los Angeles October 18-22 (the week following these scheduled meetings), it has been possible to procure ten outstanding teachers in the cancer field from the East, Midwest and Northwest. They will join an equal number of California speakers to staff the meetings.

To give complete coverage, it has been necessary to form two teams of speakers, one of which will cover the northern part of the state and the other the southern. A total of ten meetings, consisting of afternoon and evening sessions, will be held in the following cities:

Date	*Northern Team*	*Southern Team*
Monday, October 11, 1948	Redding	Bakersfield
Tuesday, October 12, 1948	Sacramento	Santa Barbara
Wednesday, October 13, 1948	Stockton	Long Beach
Thursday, October 14, 1948	Day of Rest	Day of Rest
Friday, October 15, 1948	Carmel	San Diego
Saturday, October 16, 1948	Fresno	Riverside

In addition to this announcement, individual notices will be sent out to all physicians in California during the latter part of September, reminding them again of the meetings. To make proper arrangements, it is necessary that we know about how many physicians will be in attendance at these meetings. Will you, therefore, fill in the information requested on the self-addressed return post card as soon as you receive it and get it in the mail at the earliest possible time.

C.P.S. FEE SCHEDULE TO BE REVISED

A matter of first importance to every physician in California is highlighted by a recent action of the Board of Trustees, California Physicians' Service. In a letter from Chester L. Cooley, M.D., secretary, the Board officially authorized William L. Bender, M.D., chairman of the Fee Schedule Committee, to proceed at once with the complete revision of the C.P.S. Fee Schedule.

The members of the Fee Schedule Committee are as follows:

William L. Bender, M.D., chairman, San Francisco.
Jesse L. Carr, M.D., San Francisco.
R. G. Frey, M.D., Red Bluff.
F. E. Jacobs, MD., San Diego.
John G. Manning, M.D., Los Angeles.
Frank B. Reardon, M.D., Sacramento.
S. W. Sensiba, M.D., Santa Monica.
H. J. Templeton, M.D., Oakland.
Harold P. Totten, M.D., Los Angeles
Moris Horwitz, M.D., Beverly Hills.

The Fee Schedule Committee will hold sectional meetings throughout the state. The meetings will be publicized well in advance so that interested physicians from every area may attend. All C.P.S. physician members are urged to place these meetings high on their agenda for it is imperative that the new Fee Schedule shall reflect, so far as possible, the best thinking of the entire medical profession of the state.

PROGRAM—CANCER MEETINGS

AFTERNOON SESSION

Hour	Subject	Speakers: Northern Team	Speakers: Southern Team
1:30 p. m.	Diagnosis and Management of Skin Cancer (30 min.)	Samuel Ayres, Jr., M.D., Prof. of Derm. and Syphilology, School of Dentistry, U.S.C., Los Angeles, Calif.	Sydney Thomas, M.D., Clinical instructor in Radiology, Stanford Univ. School of Medicine, Palo Alto, Calif.
2:00 p. m.	Diagnosis and Treatment of Intraoral Cancer (30 min.)	Ernest M. Daland, M.D., Ch. Staff and Surgeon, Pondsville Hospital, Walpole, Boston, Mass.	Danely P. Slaughter, M.D., Asst. Prof. of Surgery, Univ. of Illinois Medical School, Chicago, Ill.
2:30 p. m.	Surgical Biopsy—How, When and Where to do (15 min.)	John W. Budd, M.D., Pathologist, Los Angeles Tumor Institute, Los Angeles, Calif.	James F. Rinehart, M.D., Prof. Pathology, Univ. of Calif. School of Medicine, San Francisco, Calif.
2:45 p. m.	General Discussion on Radiation Treatment of Cancer (30 min.)	Lowell S. Goin, M.D., Past Pres. Radiological Society N.A., Los Angeles, Calif.	L. Henry Garland, M.D., Assoc. Prof. Radiology, Stanford Univ. School of Medicine, San Francisco, Calif.
3:15 p. m.	Recess (10 min.)		
3:25 p. m.	Diagnosis and Treatment of Cancer of the Lung (30 min.)	Michael DeBakey, M.D., Prof. of Surgery, Baylor Univ., Houston, Texas.	W. E. Adams, M.D., Prof. of Surgery, Univ. of Chicago, Chicago, Ill.
3:55 p. m.	Diagnosis and Treatment of Cancer of Colon and Rectum (30 min.)	Chas. B. Puestow, M.D., Prof. of Surgery, Univ. of Illinois Medical School, Chicago, Ill.	R. Kennedy Gilchrist, M.D., Assoc. Prof. of Surgery, Univ. of Illinois Medical School, Chicago, Ill.
4:25 p. m.	Advances in Cancer Research and Newer Methods of Cancer Therapy (20 min.)	A. H. Dowdy, M.D., Prof. of Radiology, U.C.L.A. Medical School, Los Angeles, Calif.	M. D. Shimkin, M.D., Clinical Prof. of Experimental Oncology, Univ. of Calif. School of Medicine, San Francisco, Calif.
4:45 p. m.	Questions and Answers on Afternoon's Topics (15 min.)		
5:00 p. m.	Adjourn Afternoon Session		
6:30 p. m.	Dinner Meeting—Discussion on California's Cancer Control Program	J. Homer Woolsey, M.D., Vice Chairman, Cancer Commission, Woodland, Calif.	Lyell C. Kinney, M.D., Chairman, Cancer Commission, San Diego, Calif.

EVENING SESSION

8:00 p. m.	Diagnosis and Treatment of Cancer of Uterus (Corpus and Cervix) (30 min.)	Langdon Parsons, M.D., Asst. Surgeon, Harvard Medical School, Boston, Mass.	Charles E. McLennan, M.D., Prof. of Ob. and Gyn., Stanford Univ. School of Medicine.
8:30 p. m.	Discussion on Papanicolaou-Traut Smear Technique (15 min.)	Edward M. Butt, M.D., Prof. Pathology, U.S.C., Los Angeles, Calif.	H. F. Traut, M.D., Prof. Obs. and Gyn. U.C. Med. School, San Francisco, Calif.
8:45 p. m.	Diagnosis and Treatment of Cancer of the Breast (30 min.)	Donald Trueblood, M.D., Sr. Cons. Dept. of Surgery, School of Med., Univ. of Washington, Seattle, Wash.	James E. Scarborough, M.D., Assoc. in Surgery, Emory Univ., Atlanta, Ga.
9:15 p. m.	Questions and Answers on Evening's Topics		

The program will be presented in the following cities on the dates indicated:

OCTOBER 11 Redding and Bakersfield
OCTOBER 12 Sacramento and Santa Barbara
OCTOBER 13 Stockton and Long Beach
OCTOBER 15 Carmel and San Diego
OCTOBER 16 Fresno and Riverside

NEWS and NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Members of the Alameda County Kiwanis Club are donating blood to a new blood reserve fund for underprivileged children at the blood bank of the Alameda County Medical Association. New deposits are made as blood is withdrawn for transfusions in children unable to pay for the service.

* * *

A new outpatient clinic for treatment of patients in early stages of mental illness has been opened in Berkeley, according to announcement by the State Department of Mental Hygiene. It is affiliated with the Langley Porter Clinic in San Francisco, the departments of Clinical Psychology and Psychiatric Social Work at the University of California and the Student Health Service at the University. The clinic, which is financed by Federal Government funds allotted under the National Mental Health Act, is under the direction of Dr. Portia Bell Hume, assistant professor of psychiatry at the University of California Medical School.

LOS ANGELES

Dr. Harry Goldblatt, director of the Institute of Medical Research, Cedars of Lebanon Hospital, recently was awarded the Charles Mickle Fellowship for 1948. Given annually by the University of Toronto to the member of the medical profession deemed to have done most in the preceding ten years to advance practical knowledge in medicine, the award went to Dr. Goldblatt for studies on the relationship of the kidney to arterial hypertension.

* * *

Dr. J. Walter Wilson, clinical professor of dermatology at the University of Southern California Medical School, and Dr. Orda A. Plunkett, associate professor of botany at the University of California at Los Angeles, have been awarded a silver medal by the American Medical Association for an exhibit they prepared on the identification of disease-causing fungi as an office procedure for practicing physicians.

SAN FRANCISCO

A continuation course in General Medicine, with 12 evening lectures at Toland Hall, University of California Hospital, has been announced for the period September 20 through December 6. Applications for enrollment may be made to Stacy R. Mettier, M.D., head of postgraduate instruction, Medical Extension, University of California Medical Center, San Francisco.

* * *

Dr. John C. Talbot last month was named assistant dean of the University of California Medical School. Dr. Talbot, who will also serve as chief premedical adviser, will continue as assistant professor of medicine and as a physician in the student health service.

SOLANO

Announcement of the appointment of Dr. Robert Murphy as assistant county physician to serve at the Solano County Hospital was announced recently by Dr. Peter J. Gauder, now in charge of the hospital.

TULARE

Doctors of osteopathy who are licensed to practice medicine or surgery will be eligible to appointment to the staff of the proposed Sierra View Hospital in Tulare County, according to a decision by the board of directors of the hospital district.

GENERAL

The Oregon State Medical Society, which will hold its 74th annual session at Medford, September 15-18, has invited members of the California Medical Association to attend the meeting. Programs have been sent to C.M.A. members in Northern California.

Programs of two postgraduate SYMPOSIA ON HEART DISEASE, one to be held October 27-30 by the Heart Division of the San Francisco Tuberculosis Association, the other November 4 and 5 by the Los Angeles Heart Association, are as follows:

NINETEENTH ANNUAL POSTGRADUATE SYMPOSIUM ON HEART DISEASE

October 27-30, 1948, St. Francis Hotel, San Francisco

PROGRAM

Wednesday, October 27, 1948

1:30 P.M.-5:00 P.M.

SESSIONS ON HEART DISEASE IN CHILDREN

Sponsored by the Academy of Pediatrics, Northern California

Presiding: A. L. Gleason, M.D.
Chairman for Northern California

1:30—The Diagnosis of Rheumatic Fever and Its Pitfalls—Alice Potter, M.D.
1:50—The Clinical Significance of the Anti-Streptolysin Titer in the Diagnosis of Rheumatic Fever—Lowell A. Rantz, M.D.
2:00—The Difficulty in Evaluating Systolic Murmurs in Children—Marlow Harrison, M.D.
2:20—The Management of Rheumatic Fever—Harold H. Rosenblum, M.D.
2:40—Congestive Failure in Children—Saul J. Robinson, M.D.
3:00—Recess.
3:15—The Diagnosis of Congenital Heart Disease in Infants—Ann Purdy, M.D.
3:35—Diagnostic Criteria of Operable Congenital Heart Disease—Mary B. Olney, M.D.
4:00—Newest Surgical Procedures in Operable Congenital Heart Disease—Round Table.
Moderator: Ann Purdy, M.D.
Participants: Roy Cohn, M.D., Frank Gerbode, M.D., Norman Freeman, M.D., Emile Holman, M.D., Sanford Leeds, M.D., H. Brodie Stephens, M.D.

Wednesday Evening, 8:00 P.M.

Presiding: William J. Kerr, M.D.

The Uses of the Technique of Venous Catheterization, Eugene A. Stead, Jr., M.D.

(This session is held in collaboration with the Medical Extension (University Extension), University of California Medical School, as one feature of a postgraduate series of 12 evening lectures in general medicine.)

Thursday, October 28, 1948
9:00 A.M. - 12:00 M.

Presiding: Charles A. Noble, Jr., M.D.

9:00—The Rehabilitation of the Cardiac Patient—John J. Sampson, M.D.
9:30—Iatrogenic Heart Disease—
From the Point of View of the Psychiatrist—Paul A. Gliebe, M.D.
From the Point of View of the Internist—William J. Kerr, M.D.
10:15—The Use of Electrocardiography in the Diagnosis of Myocardial Infarction With Special Emphasis on Unipolar Leads—Francis L. Chamberlain, M.D.
10:45—Recess.
11:00—Heart Disease of Pulmonary Origin—John McMichael, M.D.

2:00 P.M. - 5:00 P.M.
Presiding: William W. Newman, M.D.

2:00—Clinical Pathological Conference—Alvin Cox, M.D. and Eugene A. Stead, Jr., M.D.
2:45—Clinical Uses of Quinidine——Maurice Sokolow, M.D.
3:15—The Uses and Abuses of Mercurial Diuretics—K. A. Klinghoffer, M.D.
3:45—Recess.
4:00—Round Table Discussion—Heart Failure
Moderator: J. K. Lewis, M.D.
Participants: John McMichael, M.D., and Eugene A. Stead, Jr., M.D.

Friday, October 29, 1948
9:00 A.M. - 12:00 M.

Presiding: Edwin L. Bruck, M.D.

9:00—Occlusive Arterial Disease—Norman Freeman, M.D.
9:30—The Parenteral Use of Fluids in Patients with Heart Disease—David Rytand, M.D.
10:00—Acute Myocarditis in Infectious Diseases—Lowell A. Rantz, M.D.
10:30—Electrocardiographic Changes in Acute Infectious Disease—Irving Fine, M.D.
10:45—Recess.
11:00—Fainting—Eugene A. Stead, Jr., M.D.
1:30 P.M. - 4:15 P.M.—Panel Discussion—A Symposium on Cardiac Diagnosis.
Moderator: Arthur L. Bloomfield, M.D.
Participants:
Clinical History—Arthur Selzer, M.D.
Physical Diagnosis—Clayton D. Mote, M.D.
Venous Pressure and Circulation Time—Ellen Brown, M.D.
Fluoroscopy—Robert R. Newell, M.D.
Roentgen Kymography—L. Henry Garland, M.D.
Angiocardiography—Frank Windholz, M.D.
Electrocardiography—Robert L. Smith, Jr., M.D.
Phonocardiography—J. K. Lewis, M.D.
Oxygen Saturation Studies—Howard R. Bierman, M.D.
Cardiac Catheterization—John McMichael, M.D.
Summary—Correlation of Diagnostic Methods—Eugene A. Stead, Jr., M.D.
3:20—Recess.
3:35—Questions and Answers—(Please submit questions in writing to the Heart Division office in advance.)

Friday Evening
7:00 P.M.

Nineteenth Annual Dinner Meeting
Colonial Ballroom, St. Francis Hotel

Presiding: Arthur Selzer, M.D., Chairman

The Pharmacology of Heart Failure—John McMichael, M.D.
(Green Room open at 6:00 P.M. for cocktails)

Saturday, October 30, 1948
9:00 A.M. - 12:00 M.

San Francisco Hospital
Potrero Avenue and 22nd Street—Ward P

Presiding: J. Marion Read, M.D.

Presentation of Patients with Various Types of Heart Disease
Discussants: John McMichael, M.D., Eugene A. Stead, Jr., M.D.

EIGHTEENTH ANNUAL POSTGRADUATE SYMPOSIUM ON HEART DISEASE

LOS ANGELES HEART ASSOCIATION

November 4 and 5, 1948, Wilshire-Ebell Theatre, Los Angeles

GUEST SPEAKERS

JOHN MCMICHAEL, M. D., *London, England*
EUGENE A. STEAD, JR., M.D., *Durham, N. Carolina*

Thursday Morning, November 4

9:00—Registration.
9:30—Opening Remarks—William Paul Thompson, M.D., Chairman.
9:35—Motion Picture "Coarctation of the Aorta"—John J. Jones, M.D., Los Angeles.
10:00—Coronary Artery Disease and Its Relation To Blood Cholesterol—Morris F. Collen, M.D., Oakland.
10:30—Recess.
10:45—Obligation of the Physician in the Treatment of Bacterial Endocarditis—Lewis T. Bullock, M.D., Los Angeles.
11:15—Treatment of Cardiovascular Syphilis—Joseph M. Oyster, M.D., Los Angeles.
11:45—Discussion of preceding papers.

Thursday Afternoon

2:00—Pharmacology of Congestive Heart Failure—John McMichael, M.D., London.
2:30—Current Views on the Heart in Pregnancy—Mitchell D. Covel, M.D., Los Angeles.
3:00—Clinical Uses of Venous Catheterization—Eugene A. Stead, Jr., M.D., Durham, N. Carolina.
3:30—Recess.
3:45—Joint Discussion—Cardiac Edema—John McMichael, M.D., and Eugene A. Stead, Jr., M.D.

Friday Morning, November 5

9:30—Joint Discussion—Vascular Adjustment To Circulatory Collapse—John McMichael, M.D., and Eugene A. Stead, Jr., M.D.
10:30—Presidential Address—William Paul Thompson, M.D.
11:00—Recess.
11:15—Heart Failure of Pulmonary Origin—John McMichael, M.D.
11:45—Discussion of preceding papers.

Friday Afternoon

2:00—Diet and Surgery in Hypertension—Eugene A. Stead, Jr., M.D.
2:30—Report of Nominating Committee.
2:35—Practical Approaches to Peripheral Vascular Diseases—Travis Winsor, M.D., Los Angeles.
3:05—Recess.
3:20—Clinical Pathological Conferences. (a) Eugene A. Stead, Jr., M.D., and Alvin G. Foord, M.D., Pasadena. (b) John McMichael, M.D., and Hugh Edmondson, M.D., Los Angeles.

Friday Evening

5:00 to 7:00—Informal reception at the Ambassador Hotel Gold Room.

INFORMATION

Los Angeles Venereal Disease Survey

[*The following is taken from a report by the Department of Health, City of Los Angeles*]

During the month of October, 1947, Dr. Walter Clarke, clinical professor, School of Public Health, Harvard University, and his assistants, conducted an extensive and comprehensive survey on the problem of venereal disease control in the Los Angeles area. On March 16, 1948, at the annual luncheon meeting of the Los Angeles County Venereal Disease Council, Dr. Clarke presented the report of his findings, together with his recommendations. The following are a few of the findings and suggestions of his group.

"In two years, 1944-46, syphilis stood first and gonorrhea second among communicable diseases reported, with a two year total of 35,828 cases. In spite of our vastly improved methods of treatment, deaths due to syphilis are still numerous. In Los Angeles City only tuberculosis and pneumonia among communicable diseases cause more deaths than syphilis.

"The Health Department needs expanded services, particularly laboratory facilities and personnel, to permit it to give the assistance which private physicians and industries could use to find more and more hidden cases of syphilis, many of them in people who do not know they are infected. The Health Department needs more help from the hospitals and private physicians in fighting the venereal diseases.

"More hospitals should conduct low-fee clinics, including night sessions, for employed but medically indigent patients. Too many hospitals now fail to perform routine serological tests on all bed patients, a procedure recognized as necessary in good hospital practice. Most hospitals do not attempt to obtain from syphilis patients information which would help to find sources of infection and many do not exert themselves to bring patients back for check-up examinations after treatment.

"We suggest that a mechanism should be set up to facilitate understanding and cooperation between the County Medical Society and the official and voluntary health agencies of the area. A permanent committee on public health relations with subcommittees on venereal diseases, tuberculosis, maternity and child health and other special fields, could, with advantage, be established by the County Society. An amendment to the Medical Practice Act is proposed to prohibit all advertising by licensed physicians. An amendment to the Public Health Act is proposed to prohibit anyone not a licensed physician from diagnosing or treating any venereal disease.

"We suggest the establishment of a psychiatric service associated with the Los Angeles City Health Department, the courts, and the jail, to do what can be done to find and re-direct those sex offenders who are not already so hardened in their habits as to be beyond salvage. Every prisoner detained in jail for 48 hours or longer should be examined for all communicable diseases including syphilis and gonorrhea.

"The Venereal Disease Council may formulate a three-year plan and work to secure within that period the major improvements suggested in this study, such as institution of personal and family-life education in the schools, a woman's court, a psychiatric service for sex offenders, legislation to prohibit medical advertising, and to restrict diagnosis and treatment of venereal diseases to physicians only. The Council will need the help of all public-spirited citizens in achieving its objectives, and fortunately can count on hearty cooperation of official agencies."

MENE, MENE . . .

The current dispute between the United Automobile Workers and General Motors promises to have a far reaching effect upon the future of prepaid medical care plans. The dispute involves, among other things, the question of whether or not group insurance plans come under union bargaining rights.

The union and the national Labor Relations Board think they do. General Motors thinks they don't and the question has been appealed to the courts.

There are precedents to indicate that the court will probably decide in favor of the union and the N.L.R.B. If it does, every union in the land will demand immediate negotiations with management for employee benefits—including medical care protection.

There are certain obvious developments to be expected if group insurance is certified as a union bargaining item:

1. Pension plans, group life, disability and medical care plans will become subject to union approval or veto. Management will no longer have sole authority on selection.

2. Employer acceptance of the employee benefit as an industrial relations principle will be forced by law.

3. Standards of coverage, rate, etc., will tend to fall into a pattern dictated by union specifications.

In these circumstances it is only realistic to review what Labor thinks about medical care protection—what it considers desirable and how it should be applied. To learn what California Labor thinks about the subject, the California Physicians' Service set up a department of labor relations in 1946.

Since then the department has built up a fund of information that is definitive within the boundaries of the State of California, and at least significant nationally. The basic points of California Labor's thinking on prepaid medicine are these:

1. Medical care protection should be of the "service" type. Labor is suspicious of the indemnity because it does not actually budget medical expenses and does not protect the worker against possible additional charges.

2. The protection should be complete and cover all of the worker's actual dependents.

3. Income ceilings should be raised or abolished —preferably the latter. Governed by a one scale craft wage, Labor can see nothing but a get-rich-quick philosophy in the variable medical fee, based upon income.

4. Employers should pay a portion of the cost of medical care protection.

5. An adequate program can be provided only by Government—no private plan could underwrite it without Government assistance.

6. Pending governmental action to provide it, the best of the private plans should be endorsed and supported.

7. Medical care is not solely the doctor's problem. The patient and the nation are also concerned, and deeply concerned, with it.

The probable court action in the U.A.W.-General Motors case will lift these points of belief from the academic to the active level. What will be the probable effect? There is small doubt that urban physicians will find more and more of their patients covered by some form of so-called "health insurance." For the most part the protection will be of the service type, with a scheduled fee for specific services. Doctors who will not accept such protected patients will lose business. Rural practitioners will be similarly affected but not to the same degree immediately.

If the court decides that group medical care protection is a proper subject for collective bargaining, employers will not only have to bargain over the selection of a plan but also over the union's *demand* for a medical care or insurance program. The employer will no longer be able to refuse to discuss the matter on the ground that such a program is solely a matter for management decision. Most employers can be expected to yield to union pressure on the subject, for two reasons. First, a refusal would be costly. Second, acceptance of the union's selected plan will give a strategic advantage to the employer should the plan flop.

The plans themselves, already in a sharply competitive position one to the other, will find themselves bucking union specifications as well. This additional hurdle will kill some and force the rest to new highs of administrative efficiency. For union specifications will certainly demand the broadest benefits at the lowest possible rates.

Veritably, all concerned with medical care, including those who use it, are in for an interesting experience—and it may begin very soon.

BOOK REVIEWS

COMMUNICABLE DISEASE CONTROL. A Volume for the Health Officer and Public Health Nurse. By Gaylord W. Anderson, A.B., M.D., Ph.D., May Professor and Director, School of Public Health, University of Minnesota, and Margaret G. Arnstein, R.N., M.A., M.P.H., Assistant to the Chief, Division of Nursing, United States Public Health Service. Second Edition. New York, The Macmillan Company. 1948. $5.00.

The authors place emphasis on the factors related to the control of disease rather than to the diagnosis and treatment of the individual case. Therefore, the health worker or the practicing physician interested in epidemiology will find the work of particular value.

The first part is a discussion of the infectious processes and the factors related to the spread of disease. The section on control measures includes the standard procedures of isolation and environmental sanitation and a concise up-to-date review of the principles of immunization. The whys and hows of effective epidemiological investigation will be found of interest.

Part Two deals with the specific infectious diseases, principal consideration being given to those which are of primary importance and for which something can be done. The discussion of each disease or group is concluded by recommended action by the health officer and his staff.

The place of the newer rodenticides, ANTU and 1080, and insecticide, DDT, is discussed in relation to insect-borne infections.

The authors have interestingly and authoritatively presented the newer concepts of the control of communicable disease.

THE Rh FACTOR. In the Clinic and the Laboratory. Joseph M. Hill, M.D., and William Dameshek, M.D., Editors. Grune and Stratton, New York. $4.25.

This volume, a special issue of *Blood, the Journal of Hematology*, consists of a collection of 13 papers on the Rh factor. The volume ought to be considered an issue of the Journal because of the nature of the papers. The contributions are of value to the geneticist, the immunologist, persons interested in applied clinical laboratory procedures, the hematologist interested in the mechanisms of hemolysis and transfusion reactions, those working in the field of iso-immunization, the pediatrician, the obstetrician, the clinician and the therapeutist. The subject matter of the volume may be roughly divided into two general categories, one dealing with the more theoretical and academic aspects of the problem, and the other dealing with the more practical phases of the problem which require immediate action and are of importance to the clinician.

In the first group is to be found a short historical resume by Levine, one of the earliest contributors on the subject of the Rh factor. R. R. Race reviews the nomenclature of the British workers who use the Fisher scheme of multiple allelic arrangements of the genetic factors. Dameshek contributes a review of his researches on the mechanism of hemolysis and discusses the physiologic principles of red cell destruction, the chemical and physical factors of erythrostasis, and the functions of the spleen in hemolysis. The interrelationship between the Rh system and the A B O system in hemolytic disease of the newborn is reported by Witebsky, who gives an instance of the production of an anti-A antibody of the blocking type. One of the outstanding papers of this section is that of Hill, Haberman and Jones, who discuss hemolytic Rh immune globulins, and present convincing evidence of a third order of antibodies, which they have designated "cryptagglutinoids."

The papers of the second group deal with the more practical considerations of the subject. A paper of much practical value to the clinician, on the management of acute renal insufficiency due to incompatible transfusions, is given by Muirhead, Haley, Habermann and Hill. Davidsohn contributes a provocative paper on the relationship between the character and intensity of the Rh antibodies in the mother and the resultant variety of hemolytic disease in the newborn. The significances of these factors are correlated in terms of survival of the afflicted. A companion article by Bruce Chown presents some deviations from the usual pattern of Rh sensitization. The material he presents was obtained from an isolated controlled population. Orozco discusses the rôle of hetero-specific immunization to the A and B factors and its relationship to the etiology of erythroblastosis. The highly technical details of the treatment of hemolytic disease of the newborn by substitution or exsanguination transfusion are given from the point of view of the clinician by Wallerstein.

In general, the volume consists of worthy contributions to the subject of Rh iso-immunization. It outlines some problems for future consideration. Its true nature is evident by virtue of its being a volume of assembled papers delivered at the International Hematology and Rh Conference held in Dallas, Texas, in November, 1946.

HUMAN PHYSIOLOGY. F. R. Winton, M.D., D.Sc., Professor of Pharmacology, University College, London, and L. E. Bayliss, Ph.D., Reader in Physiology, University College, London. Third Edition with 248 Illustrations. The Blakiston Company.

The authors of this book are well known English medical scientists, who have contributed knowledge to both animal and human physiology over many years of research. The point of view is distinctly one of human physiology and the book is rich in illustrations from researches on human functions, but the authors also draw freely upon results of experiments on laboratory animals for depicting more exact and analytical studies for which the human subject is not suitable. There are 15 chapters with the traditional classification of functions more or less according to anatomical systems. There is an opening chapter entitled Physiological Activity in which are discussed the principles of muscular exercise, physiological equilibria and fatigue. Other chapters are The Circulation, The Blood and Other Body Fluids, Respiration, Digestion, etc.

It is unfortunate that the able discussion of metabolism and nutrition in chapter 6 is so far removed from the discussion of the ductless glands in chapter 15. Of the 22 pages of chapter 13 on the autonomic nervous system, 12 are devoted to the chemical transmission of the nervous impulse.

The style is lucid and interesting and the selection of subject matter has been made with the view to making the book useful to the medical practitioner. The authors have done well to include so much information in 564 pages of text matter. There are 28 pages of index. The type is clear and the paper of good quality.

TREATMENT IN GENERAL PRACTICE. By Harry Beckman, M.D., Professor of Pharmacology, Marquette University School of Medicine, Milwaukee, Wisconsin. Sixth Edition. W. B. Saunders Company, Philadelphia and London. $11.50.

Revised on an average of once every three years, this book is one of the relatively few medical works of this size written by a single author. It would of course be expected that specialists in each of the included fields might readily find fault with therapeutic details. The inexperienced medical

student, on the other hand, will often find it difficult to decide between more than one suggested method of treatment in a certain situation; from time to time he might even lose sight of the main principle. Perhaps the greatest weakness of this sort of book is that, in general, it must discuss treatment of disease: the physician treats patients.

These criticisms must not be taken too seriously. The man in general practice, to whom the book is addressed, will find much of value and interest within it. All readers will appreciate the author's easy style and light touch. The present edition of 1129 pages contains only 230 more than the first edition published 18 years ago, an astounding feat in view of the great advances since then; the most modern therapy is incorporated. The book belongs in every physician's library.

OPERATIVE GYNECOLOGY. By Harry Sturgeon Crossen, M.D., Professor Emeritus of Clinical Gynecology, Washington University School of Medicine; and Robert James Crossen, M.D., Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine. Sixth Edition—entirely revised and reset. Thirteen hundred thirty-four illustrations including thirty in color. The C. V. Mosby Company, St. Louis, 1947. $15.00.

The continued popularity of this well-known treatise on operative gynecology is demonstrated amply by the demand for a new edition, the sixth in 63 years. The present edition has been broadened mainly by the inclusion of newer aspects of the technical treatment of the various forms of genital cancer, sterility, dysmenorrhea and uterine fibroids. The book is full of useful hints in minor surgical procedures. Major technical problems are described in minute detail. In fact, there is such an abundance of technical descriptions that the less experienced may find it bewildering to decide on what method to use. This is a common fault of many technical texts, largely due to the reluctance of authors to eliminate outdated material. Crossen's treatise has grown to a thousand pages in six editions, yet its usefulness could have been enhanced by the reduction in text and the elimination of archaic illustrations. Many of the latter appeared in the first edition but by now print so poorly that they serve no graphic purpose as compared to the excellent and clear illustrations and diagrams more recently added. However, there is such abundance of graphic depiction of material and technical methods that these minor shortcomings in visual aid do not detract from the general excellence of the treatise.

The general scope of Crossen's Operative Gynecology is so well known that a detailed description hardly would be justified. It is a most useful book for any physician engaged in the treatment of women but particularly valuable for those practicing abdominal and pelvic surgery. H. L. Brooks, Jr., has discussed the intestinal tract in relation to gynecologic surgery in sufficient detail in the 17th chapter to enhance the value of this text.

NEUROANATOMY. By Fred A. Mettler, A.M., M.D., Ph.D., Associate Professor of Anatomy, College of Physicians and Surgeons, Columbia University, New York. With 357 Illustrations including 33 in color. Second Edition. The C. V. Mosby Company, 1948. $10.00.

The second edition of this standard textbook of neuroanatomy preserves all the merits of its predecessor, while bringing the work up to date and amplifying the already thorough treatment of the vascular architecture of the nervous system. The thoroughgoing treatment of the thalamic nuclei is particularly welcome in this time of great interest in the therapeutic implications of the fronto-thalamic connections.

Approximately the first half of the book is devoted to a systematic consideration of the gross anatomy of the spinal cord and brain. The structures are considered in the light of their physiological as well as their anatomical relationships. Diagrams of the fiber tracts in their functional relationships are numerous and complete; as a matter of fact their very completeness is something of an obstacle to the beginning student. One could never accuse the author of over-simplification in the interest of clarity.

The remainder of the volume presents the histological anatomy of the cord and brain in an exhaustive manner, again correlating structure with function.

The illustrations, both gross and microscopic, are really superb, and represent an untold amount of labor. In all, as a reference work on neuroanatomy the book can be unreservedly commended.

THE BIOLOGICAL STANDARDIZATION OF THE VITAMINS. By Katherine H. Coward, D.Sc., Reader in Biochemistry, University of London, Head of the Nutrition Department, Pharmaceutical Society of Great Britain. Second Edition. The Williams and Wilkins Co., Baltimore, 1947.

The second edition of the author's well known book on the bioassay of vitamins has not changed greatly from the first. This is partly due to the fact that, except for outstanding deficiencies, the vitamins continue to be a controversial subject. This book does not give what physicians desire to know about the intrinsic value of vitamins *per se* to health maintenance and to disease prevention and cure. However, it does give valuable information about how the vitamin content of foods and other materials is established in order that physicians may have reliable products at their disposal. These procedures, of course, are only for those with expert skill and special facilities.

This vitamin expert has drawn extensively on her vast experience. Part I discusses the handling of animals and details of bioassay procedures for Vitamins A, B, C, D and E. The new material here is the international standard of reference for vitamin E, and a sample of vitamin D_3 which, it is stated, may soon replace the standard for vitamin D. Part II deals with the statistical methods of refining experimental data, determining the limits of error and thus the validity of results. New material on further mathematical refinement of data has been introduced here. It does seem, however, that the increasing physical and mental energies expended on statistical analysis of biological phenomena are out of proportion to those on devising crucial experiments which would give a better understanding of them. The author recognizes the limitations of statistics, for she states that nothing is really proved by statistical treatment of results. Contrary to the author's belief that statistical analysis is very simple, the mathematics involved is probably beyond the average medical student and physician. This, however, is sauce for the routine bioassayer, and the investigator, of vitamins, for whom this book has what it takes to do their jobs acceptably.

AN INTRODUCTION TO PHYSICAL METHODS OF TREATMENT IN PSYCHIATRY. By William Sargant (M.R.C.P., D.P.M.) and Eliot Slater (F.R.C.P., D.P.M.), with a Chapter on Treatment of the Epilepsies by Denis Hill (M.R.C.P., D.P.M.). Second Edition. Baltimore, The Williams and Wilkins Company, 1948. $3.50.

This is not by any means a complete treatise on the numerous methods of somatic therapy in psychiatry. It is simply and directly written, the material well organized, the more important essentials justifiably emphasized, and is directed not so much at the experienced specialist (although he can find much of benefit to him), as at the general practitioner, student, and young clinician in psychiatry. The author's plea for more active treatment in the psychiatric wards and outpatient clinics of general hospitals should be heeded more generally.

While many psychiatrists believe in the practical value of the various somatic therapies in psychiatry and recognize that they produce beneficial effects with greater speed and greater certainty than older methods, not everyone shares the enthusiasm expressed in this volume. Much of the criticism levelled at the so-called "drastic therapies" is too generally

condemnatory merely because the treatments have been used injudiciously, ill-advisedly, and indiscriminately by a few. Objections have also been raised to such treatments as malaria, convulsive therapy, insulin coma, and leukotomy, because the theoretical justifications are not proven; but even if they are empirical, clinical observations justify them by their results.

Such methods as the insulin treatment of schizophrenia, modified insulin therapy (sub-coma type), convulsive therapy, use of chemical sedatives (bromides and barbiturates), chemical stimulants (benzedrine and thyroid), continuous sleep treatment (popular in England but rarely used in this country), the use of drugs in psychotherapy (narco-analysis and narco-synthesis by means of barbiturates or ether), the use of diet, vitamins and endocrine preparations, prefrontal leukotomy and the treatment of general paresis by malaria and penicillin are all discussed. The reported results from the literature are mentioned; practical suggestions for the selection of patients, risks and contraindications and the essential details of technique of treatment are presented. There is no mention, however, of electro-narcosis therapy, of brief stimulus convulsive therapy and of trans-orbital leukotomy, but the authors have made no pretense to cover completely this ever-widening field. The English have not yet taken up the conditioned reflex treatment of alcoholism, although it has been administered in many clinics throughout this country for several years.

The authors do not use curare as routinely as many in this country and their objections are those expressed by the inexperienced. The comment that cardiazol (metrazol) is more effective than electrical convulsion in severely agitated depressions, stuporous states, acute hallucinatory excitements and persistent paranoid states is interesting, if true. In view of the severe condemnation that the Group for the Advancement of Psychiatry has levelled at the use of outpatient electro-shock therapy, it is heartening to read that "It is often better to treat a patient with electrical shock in an out patient clinic than to admit him to hospital to receive the same treatment there."

The chapter on "Treatment of the Epilepsies" by Denis Hill is short, concise, and factual. At the time this volume was written, mesantoin and tridione had been little used in England, but by now they have an established place in the therapeutic assault on epileptic manifestations.

The authors emphasize perhaps too enthusiastically the "constitutional" background to illness, but they rightfully declare "In the coordinated totality of treatment, psychotherapy has a defined but almost inevitable part. It should indeed precede, accompany and terminate physical therapy, not only in psychiatric but all medical and surgical disorders."

This book may be well recommended.

ORGANIC FORM AND RELATED BIOLOGICAL PROBLEMS. By Samuel J. Holmes. University of California Press, Berkeley and Los Angeles. 1948. $5.00.

This is a series of papers, some of which originally appeared in the *Scientific Monthly* and others in the *Quarterly Review of Biology*. They constitute primarily an inquiry into the problems of organic form, the means by which living organisms effect their own construction, keep it in repair, of how they reform themselves, and how they maintain their morphological and physiological equilibrium. It is a lesson to medical men that the currently popular conceptions of the "organism-as-a-whole" so much emphasized through psychosomatic medicine has been accepted by biologists for many years: "Continuous integration is one of the most salient and characteristic features of life." It is a particularly broad point of view which the author presents when he states that "so far as integration at one level depends upon the same kind of causes as integration in another, the understanding of the process at one level will help to explain integrations at other levels, whether they are higher or lower in the hierarchy. . . . There might be a measure of justification, therefore, in so heretical a procedure as applying the categories of the social sciences to interpret certain kinds of biological phenomena."

The author discusses graphically the subject of the role of functioning as a building process, and emphasizes how structure is in part formed, as well as maintained, through the effects of activity. In analyzing development, two principal problems are mentioned: that of divergent differentiation and the proper arrangement of parts, both of which are regarded as a consequence of continued balancing. Regeneration is regarded by the author as an outcome of functional equilibration and he utilizes the methods of regeneration of blood to exemplify this.

In discussing cancer as a biological problem, the author postulates the following series of events: trauma by various agents, either internal or external, somatic mutation, generation of viruses, abnormal metabolism, unrestricted growth and invasiveness, and behind all these are the genetic factors conditioning all these events in varying degrees.

The final chapters deal with a description of the role of autocatalytic enzymes and their relationship to the origin of life, and to a review of the history of the theories of recapitulation as they involve phylogeny and ontogeny.

This is a most stimulating and thought-provoking volume, written with erudition and suggesting problems which should be the concern of every scientifically and biologically minded physician.

DISEASES OF THE NOSE, THROAT AND EAR—A Handbook for Students and Practitioners. By I. Simson Hall, M.B., Ch.B., Surgeon to the Royal Infirmary, Edinburgh (Department for Diseases of Nose, Throat and Ear.) With Eight Colored Plates. Fourth Edition. The Williams and Wilkins Company. 1948. $4.50.

In many respects this is an amazing, small volume that does fulfill the promises of the Prefaces of both the First and Fourth Editions. It has been brought up to date as far as use of chemotherapeutic and antibiotic agents are concerned. Other than that it still contains many practices and therapeutic procedures that are definitely outmoded.

In addition, this book, if intended to have a widespread reading clientele in the United States, should have considerable terminology changed as well as incorporating modern spelling according to our standards. The terms "cotton wool," "Mackintosh," "rigor," and several other words that are interspersed throughout the book might leave some question as to the true meaning. Also used are certain ethical proprietary names for drugs that are more or less meaningless in this country.

The paper and printing are excellent. The black and white illustrations are standard or better. Unfortunately the eight color prints are not as good reproductions as far as color is concerned as we frequently find in books of this type.

The book is a good handbook and has much to offer both the general practitioner and the specialist in the field of otorhinolaryngology.

DERMATOLOGY FOR NURSES. By G. H. Percival, M.D., F.R.C.E.P., Grand Professor of Dermatology, University of Edinburgh, and Elizabeth Toddie, S.R.N., Sister in Charge, Department of Dermatology, Royal Infirmary, Edinburgh. The Williams and Wilkins Co. 1947.

This book which is designed primarily for nurses comprises 116 pages. It is very concise and is well illustrated with excellent color plates as well as good black and white pictures. There are a number of good photomicrographs of animal parasites.

The book goes into considerable detail in the application of several types of dressings and describes a number of the more important types of medication used in dermatology.

The anatomy of the skin, definitions of lesions, and some of the more important classes of eruptions are described in a brief but effective manner.

Unfortunately, in the interest of brevity many important subjects are completely omitted and it is difficult to see how a nurse could be adequately informed on the subject of dermatology without any reference to such important subjects as syphilis, cutaneous malignancies, and pre-malignant conditions. None of these subjects is mentioned in the book. and in view of their great importance it would seem that nurses should be expected to have at least a speaking acquaintance with such serious skin conditions. The text gives a fairly adequate description of psoriasis but does not mention such equally common skin disorders as pityriasis rosea, lichen planus, and acne rosacea. Contact dermatitis, which is probably the commonest single dermatosis encountered, is dismissed in six lines except for a brief discussion of treatment. No mention is made of the technique of patch testing. Pemphigus, while not common, is certainly a skin disorder which taxes the ability of the nurse to the utmost, and no mention whatever is made of this disease. Other important subjects which are omitted include various types of skin tuberculosis, leprosy, deep fungus infections, etc.

It is unfortunate that a book which is otherwise so excellent should be characterized by these important deficiencies.

A TEXTBOOK OF MENTAL DEFICIENCY. By A. F. Tredgold, M.D., F.R.C.P., F.R.S. (Ed.), Consulting Physician to University College Hospital, London. Formerly Lecturer on Mental Deficiency, London University. The Williams and Wilkins Company. Seventh Edition, 1947.

The first edition of this well-known textbook appeared in September, 1908. The seventh edition in 1947 represents, therefore, almost 40 years during which the author has constantly revised and re-edited. It remains one of the standard and best books of its kind, and can be recommended as a textbook on the subject of mental deficiency.

The whole problem is covered in a very broad fashion. Theoretical considerations are discussed adequately and the various clinical pictures are described in detail.

The American reader must realize that this is an English textbook and that various definitions and concepts are different from those held in the United States. The English classification divides amentia into three main types: Idiocy, imbecility, and feeble-mindedness. As the author points out, the term "feeble-mindedness" as used in America, is an all inclusive term for mental deficiency, while the term "moron" corresponds generally to what is called "feeble-mindedness" in England.

The author divides amentia into two main groups: Primary and secondary. He feels that primary amentia is due to heredity and that 80 per cent of all cases are primary. Secondary amentia is due to environmental factors, and only 20 per cent of cases are placed in this group. This is a rather higher figure for heredity than given by many other authors.

The author considers these three criteria—educational, intelligence quotient, and social—differentiating the normal from the defective individual, and concludes that the social criterion is the only satisfactory one.

He likewise accepts the definition of mental deficiency as given in the English Mental Deficiency Act of 1929, which states: "Mental defectiveness means a condition of arrested or incomplete development of mind existing before the age of eighteen years, whether arising from inherent causes or induced by disease or injury." On this basis, it would seem that juvenile paresis, head trauma in adolescents, and a number of other conditions which, according to our American classification, would cause a diagnosis of psychosis rather than of mental deficiency, would have the opposite effect in England.

These points are mentioned to bring out some of the differences in fundamental concepts. The reader should make certain that he notes these points; otherwise, he may not follow the rest of the book as he should. In general, the book has been brought up to date, although there are a number of places where recent references would have been superior to some of the older ones that are given.

ILLUSTRATIVE ELECTROCARDIOGRAPHY. By Julius Burstein, A.B., M.D. Visiting electrocardiographer and Chief of the Cardiac Clinic, Morrisania City Hospital, New York; and Nathan Bloom, M.D., F.A.C.P., Associate Professor of Medicine and Chief of the Department of Electrocardiography, Medical College of Virginia (Richmond). Third Edition. D. Appleton-Century Co., Inc.

This book is an elementary descriptive monograph consisting essentially of a series of plates with an interpretation accompanying each tracing. There is minimal discussion of the fundamental electrical phenomena, and rare discussion of the mechanism—as far as it is known—for any of the electrocardiographic changes described. As such, the interpretations are empirical.

The treatment of precordial and unipolar limb leads is inadequate, and is added as an appendage in one chapter toward the end of the book. Except for three examples of multiple precordial leads in this chapter, none of the electrocardiographic plates in the book have multiple precordial leads. Most electrocardiographers using unipolar leads would disagree with the statement on page 128 that "it is only in rare instances that the standard leads will fail and the precordial leads succeed in demonstrating an abnormal pattern." No discussion of the precordial leads in bundle branch block is available in the section devoted to it, yet on page 201 in the chapter on unipolar leads, a brief statement is made to the effect that multiple precordial leads are indispensable in the differentiation of right and left bundle branch block. No information is given, however, which permits the reader to determine how to make this differentiation. The same criticism could be made in regard to ventricular strain. No description of the precordial leads in right and left ventricular strain is found in the section devoted to this abnormality, yet a statement on page 201 that multiple precordial leads are indispensable in the differentiation of right and left ventricular strain is made without further elaboration. It is apparent that the discussion of unipolar and precordial leads is added to the main body of the book, and not interwoven with the general discussion when the individual patterns are being discussed.

There is a chapter on the phonocardiogram and one on radiology of the heart, which, while of value, are not directly concerned with the title of the book.

The book will be useful to beginners in electrocardiography as a compact, graphic description of the ordinary electrocardiographic patterns and the more common arrhythmias, as found in the three standard leads and in the single apical precordial lead. It cannot be considered as an up-to-date monograph incorporating the present concepts of unipolar precordial and extremity leads.

REFRESHER COURSE IN MALE HORMONE THERAPY. The Ciba Pharmaceutical Products, Inc., Summit, N. J.

This is a very handy, concise book with a fairly complete collection of excerpts and abstracts from articles contributed by investigators and clinicians in the male hormone field. The bibliography for each article is given in full. Unfortunately the data included dates only from 1940, before which time there were, of course, many essential and basic contributions to this subject. The physician will find this volume of considerable value but should supplement these abstracts with a perusal of the orginal texts. He should also remember that the name given for the hormone in the text is a trade name and not the only preparation of this particular substance.

MEDICAL JURISPRUDENCE

PEART, BARATY & HASSARD *of the California Bar*

In *Housman v. Board of Medical Examiners*, 84 A.C.A. 394, petitioner had applied to the Board of Medical Examiners for restoration of his license to practice medicine and surgery. The license had been revoked in 1941 because of the petitioner's conviction of a felony. His petition set forth his incarceration at San Quentin, his release in December of 1942, and his claimed rehabilitation. He filed his petition for a reinstatement under *Section 2376.5 of the Business and Professions Code*, which had been enacted by the California State Legislature in 1943. This section provides, among other things, that:

"A person whose certificate has been revoked or suspended for more than one year may petition the Board to reinstate the certificate after a period of not less than one year has elapsed from the date of the revocation or suspension."

The law provides that, in determining whether the petition should be granted, the Board may investigate and consider all activities of the petitioner since the disciplinary action was taken against him; the offense for which he was disciplined; his activity during the time his certificate was in good standing and his general reputation for truth, professional ability and good character. The Board denied the application for restoration of the petitioner's license, whereupon the petitioner asked the court to issue a writ of mandate to compel the Board to restore it. The trial court held that the Board had not abused its discretion and had not acted arbitrarily, and it sustained a demurrer to the petition without leave to amend.

In considering the evidence received by the Board and that presented at the court hearing, the District Court of Appeal in this case upheld the judgment of the trial court that the Board of Medical Examiners should not be compelled to restore the license of the petitioner.

The District Court of Appeal in examining the evidence that had been presented at the hearing and at the trial concluded that the petitioner had not shown the degree of rehabilitation contemplated by *Section 2376.5 of the Business and Professions Code*. Although the petitioner introduced a Superior Court certificate of rehabilitation, letters and testimony of a number of doctors, former patients and acquaintances, all of whom stated, in effect, that in their opinion petitioner was honest, conscientious, skillful, competent and ethical in his profession, nevertheless these witnesses for the most part, the court stated, showed a very limited knowledge of his activities and associations since his release from prison, their contacts being confined to infrequent meetings of a casual nature. Further, the District Court of Appeal held that the essential criterion to judge whether the petitioner had been so rehabilitated as to compel his re-admission to the Medical Profession was his own actions since his release from prison. In determining these actions and activities, petitioner, when asked "how would you characterize your activities as far as business is concerned during this interval since you left San Quentin" replied, "I have been attending to my own business, if that is what you mean"; the evidence showed that petitioner had spent considerable time in the study of medicine and had devoted himself primarily to taking care of his own financial affairs, and his father's estate and income tax adjustments. The court pointed out that during the war period, when there was a tremendous shortage of man power in war work and industry, petitioner contented himself with looking after his own financial interests and in enjoying himself at his club, and the race track. Further, the court, in its opinion, set forth the fact that while the petitioner "stated to the Board that he desired his license restored, so that he could offer his services as a physician to the Armed Forces, it was necessary for him first to demonstrate his real desire to help his country and to prove his own moral qualification to accept such a position by engaging in some work, or voluntary service, while awaiting the time when his license might be restored to him."

Then the court cited the case of a professional man who had accepted very humble employment at modest wages and had thus rehabilitated himself. The court concluded by saying that "viewing the evidence in a light most favorable to petitioner, it would seem that, at most, it can only be said that since his release, he has committed no further offenses and has been involved in no trouble. Rehabilitation would appear to require some positive action." Therefore, the District Court of Appeal held that the petitioner was not entitled to the writ of mandate. The California Supreme Court denied a petition for rehearing.





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*Viggiano, F. A.: Dysmenorrhea in Industry—Treatment with a New Antispasmodic, Indust. Med. **15**:632 (Nov.) 1946.

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Tales and Details



Waiting room chatter between fond mamas (with one eye on their wriggling offspring) can be pretty funny — and enlightening, too!

While waiting for one of my doctors, not long ago, I overheard a gal confide to the woman next to her, "This is his last shot—thank goodness, it takes only three!"

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MEDICINE, SURGERY BRING FEW CURES IN ULCERATIVE COLITIS

Following an intensive study of 100 carefully selected patients suffering from ulcerative colitis, four Chicago doctors concluded that both medical and surgical treatment bring about few specific cures.

Writing in a recent issue of *The Journal of the American Medical Association,* the doctors—Joseph B. Kirsner, Walter Lincoln Palmer, S. N. Maimon, and W. E. Ricketts—said that "it is apparent from this study that the number of 'cures' is small; in the 100 cases there are only six which we were willing to so designate."

Colitis is an inflammation of the colon. Symptoms of ulcerative colitis, termed a chronic disease, usually consist of diarrhea, cramping abdominal distress, fever, and weakness. Profuse bleeding may occur.

"Complete and lasting cure following medical management is rare. After medical management alone, it has been possible to maintain 47 per cent of the patients in a 'satisfactory' state of health; 19 per cent, though not markedly improved, are, on the other hand, not significantly incapacitated," the article says, adding:

"In spite of the emphasis on the severity of the disease, ulcerative colitis may exist for many years without significant disability and with rather minor symptoms."

The doctors found that in many cases the disease attacks the colon with greatest intensity early in the period of illness and that mortality is highest during the first one or two years.

"The cause of ulcerative colitis remains obscure. No specific organism has been established conclusively. There is no convincing evidence that the disease is psychogenic in origin. Nevertheless, it would appear from the frequent coincidence of emotional disturbance and the recurrences of symptoms that some relationship does exist."

Eighteen patients were interviewed by psychiatrists and 16 by a physician investigating the psychosomatic aspects of ulcerative colitis. Significant emotional problems were detected in 32 of the 34. Among the remaining cases, definite emotional disturbances were found in 15 and lesser degrees of emotional tension in 20.

"The patients were described by the psychiatrists as immature, dependent, and overtly passive. Anxiety states, insecurity, hostility, sexual maladjustments, schizoid tendencies were commonly observed. There was a tendency for the symptoms to recur or to become accentuated during the development of situations requiring responsible and decisive action."

Eighty-one patients were treated medically throughout their illness and 19 patients were treated surgically. Twenty-five of the first group and three of the second showed marked improvement.

The study shows that persons between the ages of 10 and 40 years are most often affected, but that the disease may occur at any age.

"The effect of more modern methods of therapy (nutritional, antibiotic, psychiatric) on the course of the disease remains to be ascertained," the writers comment.

44...

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Colitis[2]
Biliary dyskinesio

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DISINFECTANT ON HANDKERCHIEFS MAY HELP KEEP COLDS FROM SPREADING

Using a disinfectant on handkerchiefs might be one step toward preventing the "common cold" from spreading, according to the London correspondent of *The Journal of the American Medical Association,* writing in a recent issue.

Reporting on a lecture by Dr. C. H. Andrewes, F.R.S., of the National Institute for Medical Research, on recent research on the common cold, *The Journal's* correspondent said that "some recent evidence suggested that more unpleasant germs were spread from the nose than from the mouth and throat, which led to the question whether bacteria and viruses accidentally shaken from handkerchiefs might not be of great importance. Tests showed that many bacteria might be shaken out and remain in the air. Handkerchiefs from the later stages of colds were found to be particularly effective as germ distributors. Work now in progress suggested that impregnation of handkerchiefs with a disinfectant might make them much less dangerous in this respect."

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EMERSON, *Art.*

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FIGURE 1 — Patient — thin type of build with beginning faulty body mechanics. The Camp adjustment provides a more stable pelvis, allowing patient to "draw in" the abdominal muscles thus gradually acquiring a gentle lumbar curve.

FIGURE 2 — Patient — intermediate type of build. Strain of lumbosacral joint predisposes to other strains. For protection of the joints in the lumbar region from recurrent strain and also as an aid in relieving the pain of acute conditions, Camp lumbosacral supports have proved effective.

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POLIOMYELITIS IN SAN FRANCISCO—1930-1947

Morbidity reports for poliomyelitis are not sufficiently complete to determine distribution of cases in all racial groups, the San Francisco Department of Public Health reports, but an attempt to find cases of poliomyelitis among the Orientals resulted as follows: In the epidemic of 1930, of the 230 cases reported, 11 were in Chinese and two in Japanese. During the remainder of the 18-year period covered, no other cases among the Japanese were found and for the Chinese there was one case in 1931, one in 1934, and two in 1945. The period was of sufficient duration and the check sufficiently accurate to justify the conclusion that the Oriental population was not affected to any significant extent by the spread of poliomyelitis either during normal or epidemic years.

During the 18-year period, a total of 864 cases of poliomyelitis were reported, 481, or 56 per cent, in males; 383, or 44 per cent, in females. In 1930, during the period the severest epidemic, 87 per cent of the cases were in the age group under 25 years, distributed as to sex, 129, or 64 per cent male; 72, or 36 per cent, female. During this year the population under 25 years was distributed as to sex, 51 per cent, male, 49 per cent female, indicating a much higher incidence of poliomyelitis in the male group. The case rate in this epidemic was: in males, 122 per 100,000 population; in females, 70. A similar check of the last epidemic period, 1945, again shows 87 per cent of the cases were in the under 25 age group, males 42, or 54 per cent; females 36, or 46 per cent. The population figure for this year did not include service personnel, so that distribution as to sex in the population was male 46 per cent, female 54 per cent. The incidence of poliomyelitis was still much higher for the male group than for the female, and the case rates in 1945 were 41 in 100,000 population, males, and 30 per 100,000 for females.

A study of incidence by age groups reveals that in both normal and epidemic years the highest proportion of cases, about 35 per cent, fall within the 5-9 age group. High incidence in male groups under 25 years does not carry over into the over-25-year group. In both epidemic and normal years of incidence the percentage of females in that group is double that of the males.

Although no epidemic has reached its peak prior to June 1 in San Francisco, the seasonal incidence is neither fixed nor predictable. Experience has demonstrated that the disease flourishes in warm weather, the periods of elevated incidence often coinciding with periods of annual maximum temperatures.

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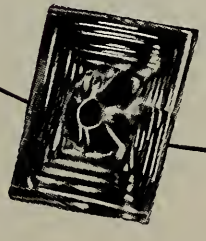
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HOUSE DUST MAY CAUSE INFANTILE ECZEMA

The possibility that house dust is an important cause of atopic dermatitis, or infantile eczema, is advanced by Jerome Glaser, M.D., of Rochester, N. Y., writing in a recent issue of *The Journal of the American Medical Association.*

Infantile eczema is an allergy disease which, it is believed, is caused by direct contact of the skin with certain allergens, as well as by allergens which have been inhaled and which reach the skin through the blood stream. An allergen is any substance which is capable of inducing allergy or specific susceptibility.

Among the characteristics of atopic dermatitis are watery sores, scales and crusts, and itching or burning sensations. The affliction is commoner in infants and children because their tender skins are more easily penetrated by allergens than those of adults.

According to Dr. Glaser, "the characteristic distribution of atopic dermatitis, with lesions worse on the face, the area of the arms below the elbows and the area of the legs below the knees, suggests a possible contact origin." In view of this, he says, "it is tempting to consider that such lesions might be caused by a ubiquitous and powerful allergen, house dust, which could act either by contact or inhalation."

As further evidence of the importance of house dust in causing infantile eczema, Dr. Glaser points out that "the often remarkably beneficial results of hospitalization are commonly attributed to avoid-

(Continued on Page 46)



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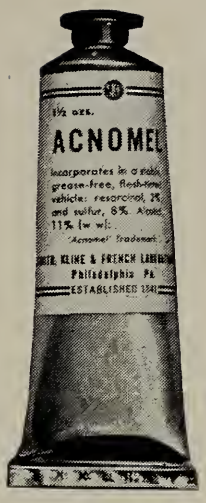
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HOUSE DUST MAY CAUSE INFANTILE ECZEMA

(Continued from Page 42)

ance of house dust as well as other environmental allergens," adding that good results in the alleviation of the condition have also been attained by treating patients with injections of house dust extract.

According to the article, there is no completely satisfactory treatment of infantile eczema and therefore "the problem is to do the best one can with a disease which is usually self-limited, with a tendency to spontaneous remissions and eventual recovery regardless of therapy."

Prophylactic, or preventive measures, such as avoidance of dust or irritating wool clothing, are considered important in the orthodox treatment of the disease. Special baths, prepared by adding a cup or two of cornstarch to a tub of tepid water, are also recommended for early stages of the disease.

The local application of paste of resorcinol, made up of one part zinc oxide, one part corn or arrowroot starch, and two parts white petroleum is highly satisfactory in more advanced or chronic stages. In all cases of atopic dermatitis, the article says, it is well to put the patient on a simple elimination diet, which includes substitutes for cow's milk and the administration of vitamins A, D and C.

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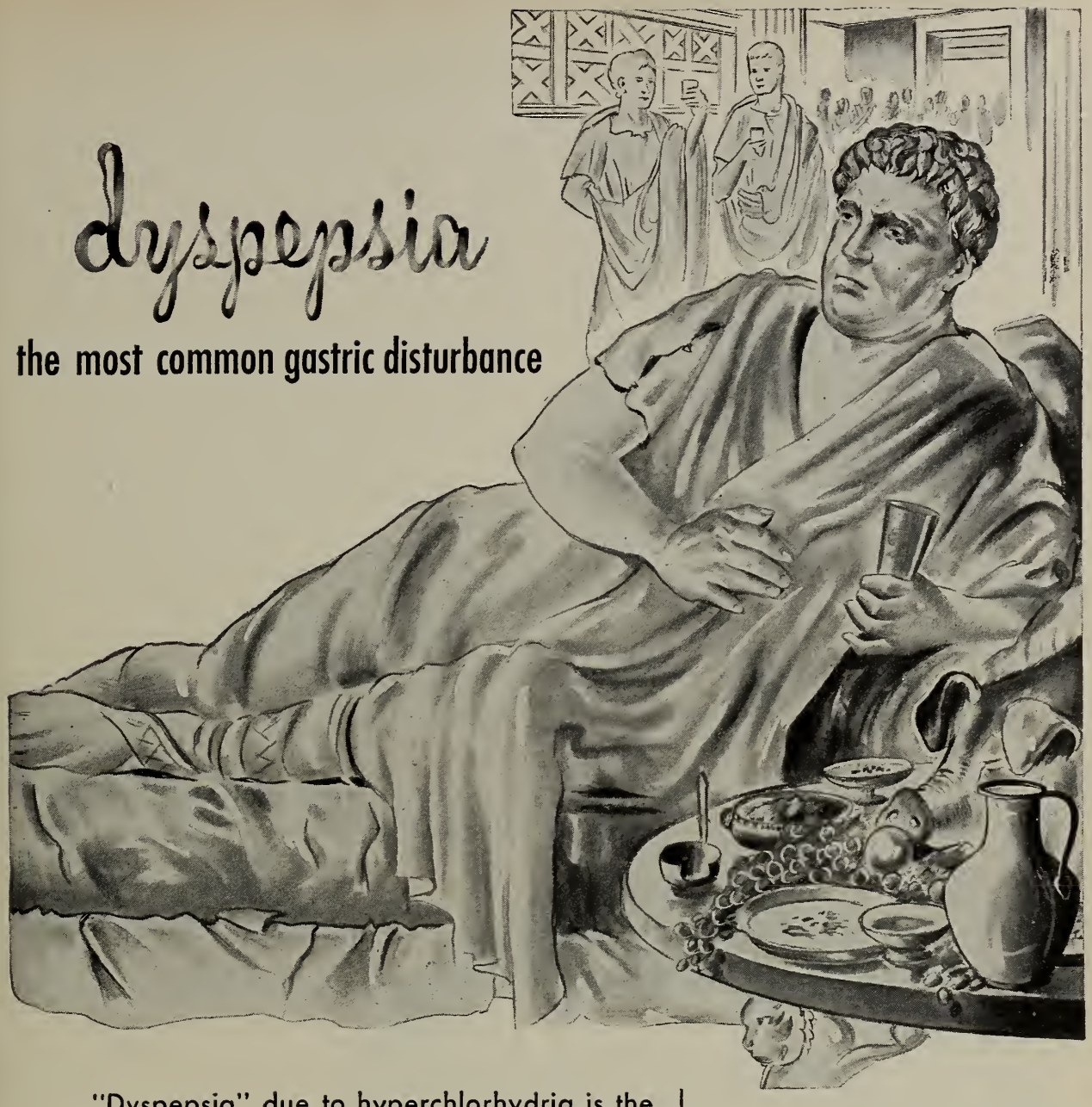
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SURGERY FOR FACIAL PARALYSIS DESCRIBED BY CHICAGO DOCTOR

Several technics for the surgical repair of facial paralysis are described by Paul W. Greeley, M.D., Chicago, in the current issue of the *Archives of Surgery*, published by the American Medical Association.

Facial paralysis may result from injury to the seventh, or facial nerve. This nerve may be damaged in several ways, including skull fracture, bullet wounds, injury from a mastoid operation, or tumors on the nerve.

According to Dr. Greeley, the best method of repair involves surgery of the injured nerve, with the intention of permitting the face to gain motion again. This may include the sewing together of the ends of the lacerated nerve trunk or the grafting of part of one nerve to another to fill in a gap if the injury made one.

The uniting of one nerve to another, which has been used several times in the treatment of facial paralysis, is undesirable, the report says, because "the associated movements involved in trying to move the facial muscles are awkward and frequently more conspicuous than the original facial paralysis."

When nerve surgery cannot be undertaken, the article says that "the simplest and most satisfactory plastic surgical correction is obtained by supporting the paralyzed face with strips of autogenous fascia lata."

This procedure involves transplanting the strips of tissue under the skin from the muscle of the

(Continued on Page 54)

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(Continued from Page 50)

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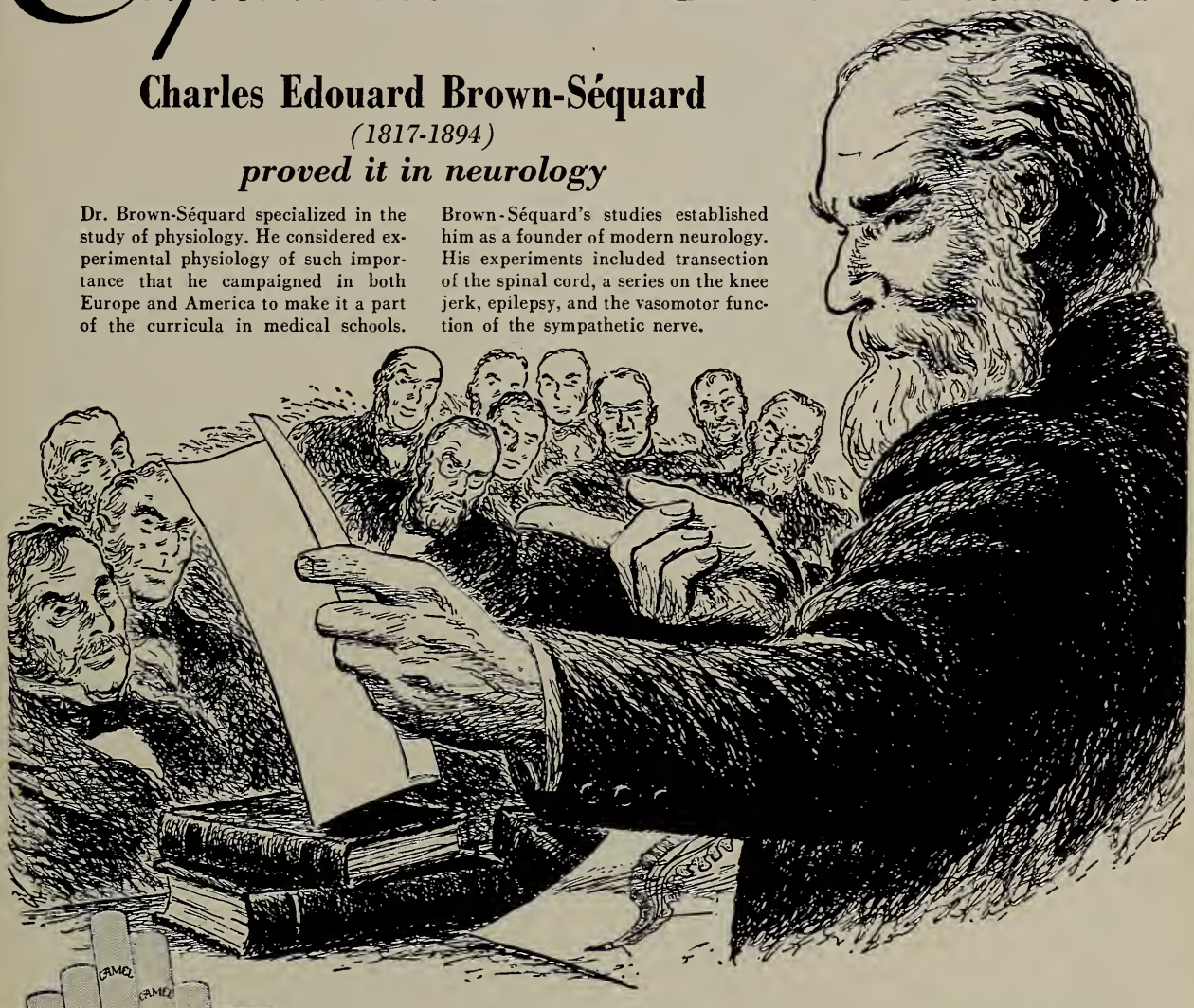
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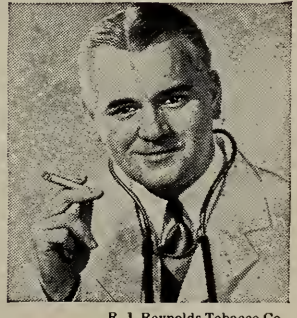


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GENERAL HEALTH HAS LITTLE EFFECT ON TOOTH DECAY

Observing that a group of Filipino children in poor general health had much better teeth than a group of local children in Hawaii in excellent health, Dr. Nils P. Larsen, Honolulu, says in the current issue of *The Journal of the American Medical Association* that dietary factors are probably the determining element in freedom from tooth decay.

Dr. Larsen's paper, entitled "Tooth Decay in Relation to Diet and General Health," was based on extensive studies made of more than 1,000 children living on sugar plantations in Hawaii and 100 children who were brought in from the war-torn Philippines.

Although tooth decay in general is higher among children on a diet with a high carbohydrate content —that is, one of starches and sweets—Dr. Larsen emphasized that this is not always the case—that some children on such diets have very good teeth.

The reported observations in Hawaii suggest that other factors than the acid base balance or vitamin A may account for the striking difference in decay in the various groups of children observed.

"Heredity," he says, "does not seem to play an important role in this condition. Hawaiians on the Polynesian diet for 800 years had excellent teeth, while first generation Hawaiians on the Oriental diet of rice had poor teeth. Filipino children in the Philippine had little tooth decay, while Filipino children in Hawaii had much."

Indications are, Dr. Larsen said, that it is not sugar or vitamin intake themselves which determine tooth decay or lack of it, but rather whether certain protective substances, such as fluorine or oxalate, are added to the diet.

"The Hawaiians on their ancient diets consumed much seafood which is high in fluorine," Dr. Larsen says. "They probably also swallowed more ocean water, which is high in fluorine. They also ate much taro and poi which is high in oxalate—a possible tooth decay preventive, as might be vitamin K which is present in raw sugar cane."

Dr. Larsen indicated the possibilities are strong that peoples with the best teeth are those whose diet consists of a combination of foods whose chemical makeup prevents the overactivity of acid-forming bacteria. Such diets contain not only fluorine and oxalate, but foods with a high alkaline residue.



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X-RAYS FOUND EFFECTIVE IN DISEASE OF LYMPH GLANDS

X-rays have been found very helpful in the treatment of a comparatively newly described disease of the lymph glands, according to Dr. Sidney Rubenfeld, of the Department of Radiation Therapy, Bellevue Hospital, New York.

Writing in a recent issue of *The Journal of The American Medical Association*, Dr. Rubenfeld reports a fairly high percentage of treated patients who have survived five years or more.

The lymph gland disease which *The Journal* article describes is known medically as giant follicular lymphadenopathy or Brill-Symmers disease, named after Nathan E. Brill, a New York physician who died in 1925, and Douglas Symmers, a New York pathologist.

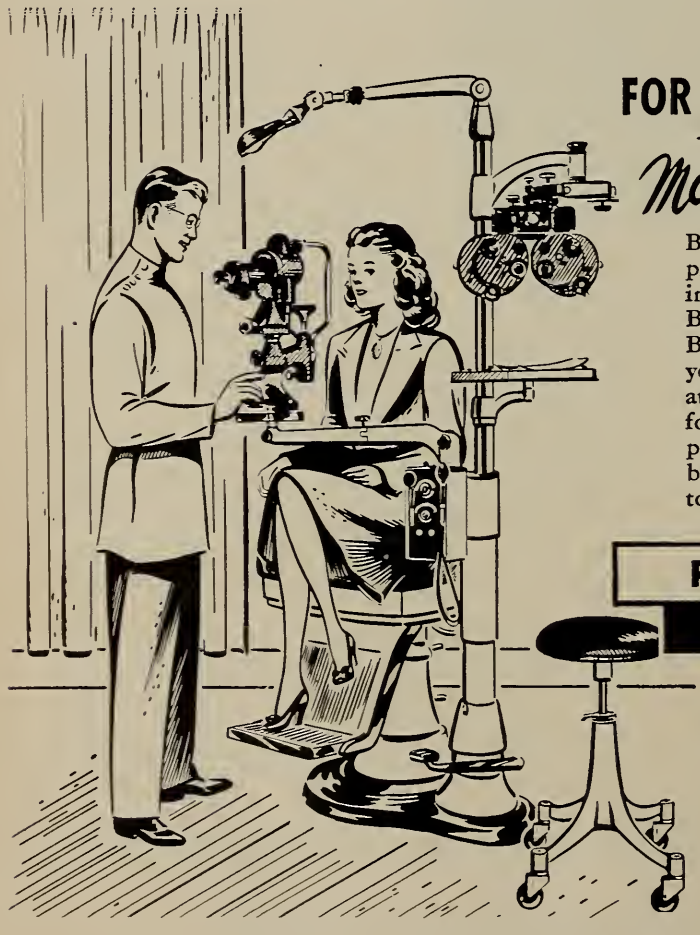
The disease is characterized by enlargement of the lymph nodes in various parts of the body and enlargement of the spleen, these enlargements being due to the abnormal multiplication of normal cells within the lymph nodes. These nodes are tiny organs scattered in many parts of the body, especially in the neck, armpits, around the roots of the lungs, around the intestines and in the groins.

This disease, the article says, has been "widely recognized by pathologists but is only beginning to attract the attention of clinicians, among whom it is almost always mistaken for Hodgkin's disease. Both are primarily diseases of the lymphoid system."

(Continued on Page 66)

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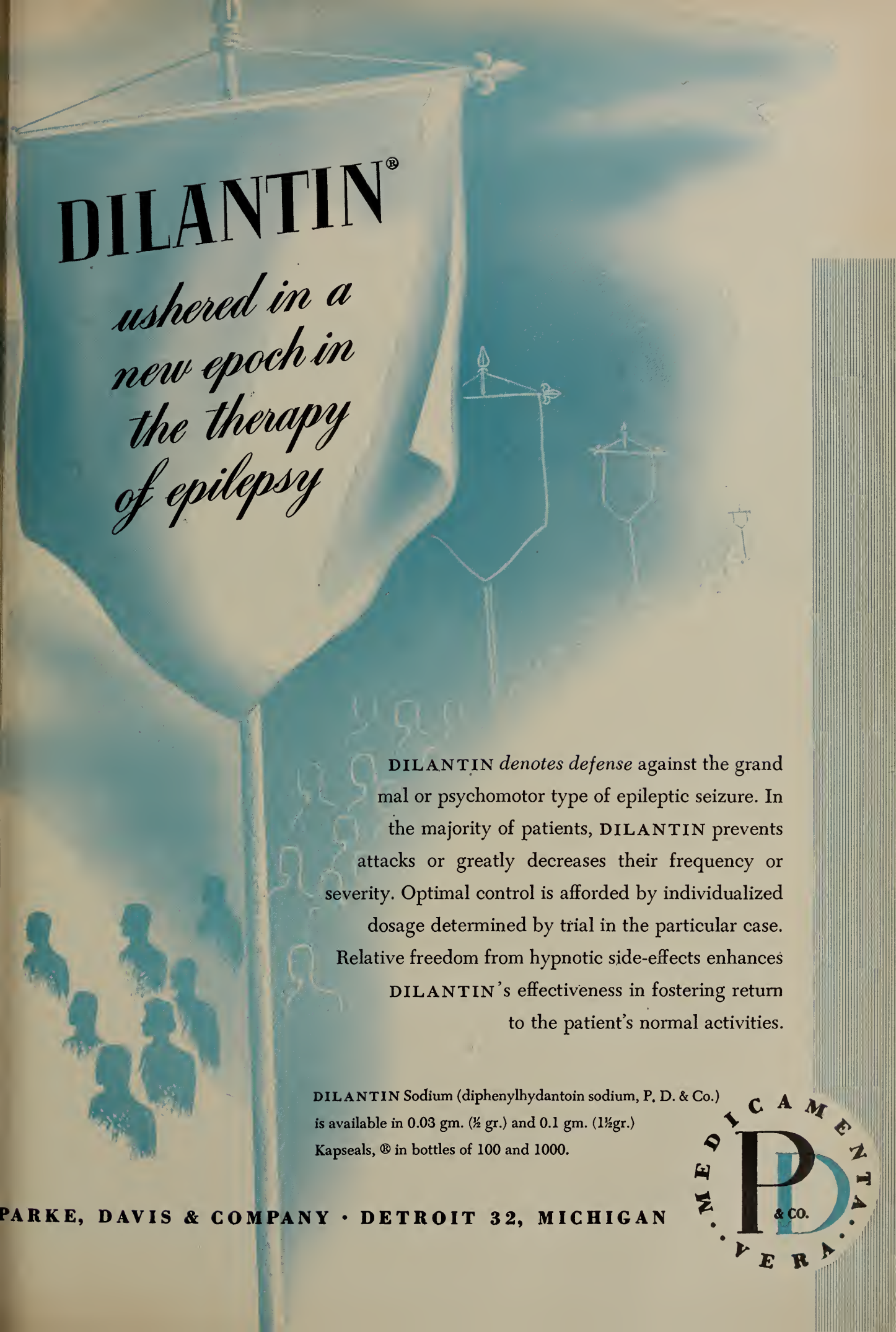
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X-RAYS FOUND EFFECTIVE IN DISEASE OF LYMPH GLANDS

(Continued from Page 62)

Dr. Rubenfeld's paper was based on a study of 19 patients with giant follicular lymphadenopathy or with polymorphous cell sarcoma, which is a highly malignant tumor containing cells of several varieties. The oldest patient was 59, the youngest 12. There were five females and 14 males. Enlarged lymph nodes constituted the outstanding clinical feature.

X-rays were used in the treatment of all 19 patients.

"In addition to the difference in the degree of response there were variations in the rapidity of the recession," the doctor pointed out.

Sixty-six per cent of patients with giant follicular lymphadenopathy and 60 per cent of those with polymorphous cell sarcoma are apparently well five or more years after the institution of treatment, the article says.

Heretofore, five year survival rates for diseases of this kind were quoted in the medical literature at only 47 to 50 per cent.

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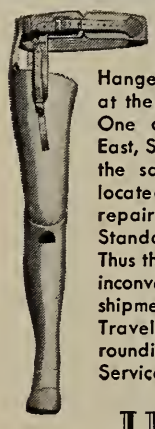
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TESTS NEW METHOD OF IMMUNIZING FOR DIPHTHERIA AND WHOOPING COUGH

A comparatively new method of immunizing children against diphtheria and whooping cough gives better protection from diphtheria than immunizing against the disease separately and "confers substantial protection" against whooping cough, according to Dr. Joseph A. Bell, senior surgeon of the United States Public Health Service at Bethesda, Md.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Bell describes immunization against diphtheria in a fully controlled clinical test of the method which was begun in Norfolk, Va., and nearby territory in 1941. His article describing immunization against whooping cough in the test will appear in a forthcoming issue of the *Journal*.

The method consists of injecting an alum-treated mixture of whooping cough vaccine and diphtheria toxoid in two doses, four weeks apart. Its worth in preventing epidemics of the disease is indicated by the simplification of the manner of immunization and by the increased protective value against diphtheria.

The injections are effective in babies as young as two to five months of age against both diseases, Dr. Bell says, and side reactions are "few and negligible."

Diphtheria toxoid is the poison developed by diphtheria germs, which, when treated with alum or another substance so that it is not harmful, stimulates the body to build up resistance against the disease. The alum-treated type of toxoid has been recognized since 1940 for immunization against diphtheria. The whooping cough vaccine used in the mixture is one selected by Dr. Bell as "promising for general use."

Assisted by the Norfolk City Union of the King's Daughters Visiting Nurse Association and the state and local health departments and physicians, Dr. Bell tested children from the ages of 2 months to 23 months selected to be representative of children in any sizable community in the nation.

To insure accuracy of the results, the children were divided at random into test groups which received the mixed product and control groups which received the unmixed products.

Among the 407 children who received two doses of the mixed product, 48 cases of whooping cough occurred; among the 385 children who received two doses of the vaccine alone, 158 cases of whooping cough occurred.

A year after receiving the first injection, 992 children in the diphtheria study were given Schick tests, the standard method of determining resistance to diphtheria. Children who received the mixed product has only one-third as many Schick-positive reactions, showing susceptibility to diphtheria, as did those who received the unmixed toxoid.

At least one of the doses should be given after a child is six months old, whether the mixed product or only the toxoid is used, Dr. Bell points out.

"It is significant that children who received both their doses before they were six months of age had a higher proportion of Schick positive reactions than those who received at least one of their doses when they were six months of age or over."

(Continued on Page 12)



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(Continued from Page 10)

But the mixed product is more effective even when given before the child is six months old than is the toxoid alone when given at any age under one year, Dr. Bell says.

The importance of receiving two doses was also brought out by the study. Children who received only one dose of either the mixed product or the toxoid were only immunized one-third as well as were children who received two doses.

The average annual attack rate of whooping cough in children who received two doses of the mixed product was slightly more than 3 per cent, while that of children who received only one dose of the mixed product was slightly more than 8 per cent, according to Dr. Bell.

Further analyses, which will be discussed in future reports, show that the rate in children who received no whooping cough vaccine was about 11 per cent and in children who received three doses of whooping cough vaccine outside the study was about 4 per cent, he says.

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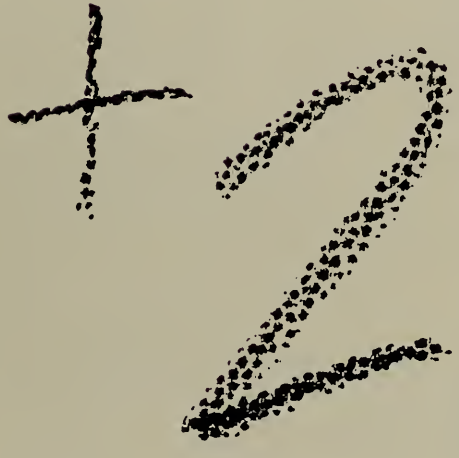
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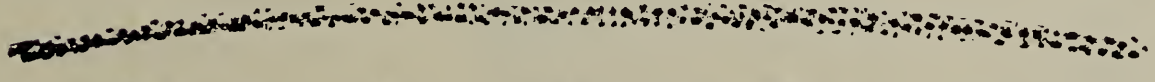
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FIND HISTAMINE VALUABLE IN TREATING MIGRAINE HEADACHE

Histamine, a body tissue chemical thought to cause many allergic reactions, is valuable in preventing and treating migraine headache, report two physicians of the Mayo Clinic at Rochester, Minn.

Writing in a recent issue of *The Journal of the American Medical Association*, the physicians—Dorothy Macy, Jr., and Bayard T. Horton—describe a study of the use of histamine in treating migraine headache at the Mayo Clinic from 1937 to 1946.

Histamine, which has no narcotic effect, was given by injecting beneath the skin and by dripping into the veins. "The greatest improvements occurred among the patients receiving histamine by both routes," the article points out.

The physicians divided the 144 patients studied into typical and nontypical cases. Both kinds showed periodic headaches, but in addition the typical cases had at least two of the following symptoms while the nontypical cases had only one: (1) Upset stomach, (2) brain disturbance, and (3) a family history of migraine.

Headaches caused only by psychic factors and nervous tension were not considered migraine, although nervous tension is frequently one of the symptoms of the disease. True migraine, as regarded

(Continued on Page 17)

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FIND HISTAMINE VALUABLE IN TREATING MIGRAINE HEADACHE

(Continued from Page 16)

in the study, is a condition of constriction of the blood vessels followed by dilation which often produces swelling.

Of the 144 patients 98 showed 25 to 100 per cent improvement. However, the treatment is not a cure, the physicians emphasize.

"The duration of freedom from migrainous attacks parallels rather exactly the duration of administration of adequate maintenance doses of histamine. Patients free of symptoms after one year or more were still taking histamine once daily or every other day."

ALTITUDE OF 8,000 FEET DOES NOT INJURE HEART

Contrary to widespread belief, living at an altitude as high as 8,000 feet is not injurious to the heart, says Gonzalo Esguerra Gomez, M.D., of Bogota, Colombia.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Gomez bases his conclusion on a study of 480 residents of Bogota, which is 8,016 feet above sea level. In none of these residents did he find enlargement of the heart out of proportion to the general build or abnormal variations in blood pressure, pulse, respiration, or number of red blood cells.

Prolonged strenuous exercise can cause enlargement of the heart, he says, but no more so at 8,000 feet than at sea level.

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TWO NEW PROCEDURES AID DIAGNOSIS OF CANCER

Two relatively new laboratory and clinical procedures aid the diagnosis of cancer and appear to be valuable in cancer research.

By transplanting tissue from human beings to the eye of a guinea pig, growths which are still "precancerous" can be distinguished from those which have reached the state in which metastasis—spreading to other parts of the body—may occur, says Harry S. N. Greene, M.D., of the departments of pathology and surgery, Yale University School of Medicine, New Haven, Conn.

A procedure of extracting marrow from the hip bone aids in diagnosing certain types of cancer and provides readily accessible material which may be useful in cancer research, according to Michael A. Rubinstein, M.D., of the Montefiore Hospital, New York, N.Y.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Greene describes the technique of transplanting human tumors as "simple" and says that since only embryonic tissue and cancer tissue survive transfer from one species to another, growth after transplanting immediately identifies the tumor in question as cancer.

The form in which a transplant from a metastasized cancer grows enables him to discover the tissue or organ from which the disease originated, he reports.

(Continued on Page 24)

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MINOR HEALTH BENEFITS IN SUNBATHING, SAYS HYGEIA ARTICLE

Sunbathing is less beneficial than many people think, according to an article appearing in the current issue of *Hygeia,* health magazine of the American Medical Association.

The article, entitled "Sunshine is Less Important than You Think," was written by Vivian Vieweger, who is currently engaged in writing a novel with a scientific background at her home in Houston, Texas. Miss Vieweger studied medicine at Washington University School of Medicine and was research assistant in the department of preventive medicine of the Johns Hopkins University School of Medicine.

Benefits of sunlight—sterilization of the skin and surrounding air, increase of vitamin D in the body, and a psychic "lift"—are insignficant when compared to the dangers of oxerexposure, she warns.

"There is a tendency to exaggerate the vital importance of sunlight. Blistered sun worshipers put a strain on their kidneys, may develop toxemia or shock, and even die. People with an unstable nervous system, an overactive thyroid gland, high blood pressure, heart disease, or active tuberculosis must be especially careful about getting an overdose of sunshine," says Miss Vieweger.

"What most people do not realize is that they can obtain the ultraviolet rays without being in direct sunlight. Riding in a car or sitting at an open window on a summer's day will benefit you from the ultraviolet radiations from the sky," she continues.

Ultraviolet rays are responsible for burning and tanning, but also help to prevent rickets by stimulating the production of vitamin D in the skin.

Emphasizing the relationship between exposure to sunlight and skin cancer, Miss Vieweger reports that the disease is eight times as frequent among men of the U. S. Navy as among the general population, has a high incidence among outdoor workers such as farmers and fishermen, is most common in regions which have strong sunlight during a large portion of the year, and is rare among dark-skinned races.

"But even if too much sunlight does not produce a skin cancer," she says, "it may cause a large number of the red blood corpuscles to dissolve and to liberate two chemicals. One of these, called porphyrin, is photodynamic—that is, it makes the sunlight's effects more damaging to the tissues.

"The second chemical is histamine. Histamine is thought to be responsible for the itching and blistering and even for the actual sickness that may follow sunburn. People have died from inflamed skins, nerve damage, delirium, and general intoxication following overexposure to tropical sunlight. Their deaths have been blamed on histamine."

What can you do to protect yourself against the sun? Most antisunburn preparations now on the market give some protection, but the more attractive the preparation the less useful it usually proves, advises Miss Vieweger.

Yellow and white petrolatum jelly are effective, and formulas for a druggist to make up can be obtained from the U. S. Public Health Service, she says.

For the average person who tans readily, Miss Vieweger's formula is: "When the skin begins to

(Continued on Page 24)



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MINOR HEALTH BENEFITS IN SUNBATHING, SAYS HYGEIA ARTICLE

(Continued from Page 22)

turn pink it is high time to get out of the sun." Ten minutes longer may produce a painful blister, she emphasizes, adding:

"People with tender skins will have to be doubly careful at the waterfront, on beaches and boats, or skiing in the snow; ultraviolet exposure increases with reflection from snow, ice, and water. It also increases with altitude.

"Just as important as sunlight are rest, fresh air, proper diet, congenial occupation, and favorable environment.

TWO NEW PROCEDURES AID DIAGNOSIS OF CANCER

(Continued from Page 20)

The guinea pig test is more reliable for determining the type of cancer than is examination of a specimen under the microscope, he indicates.

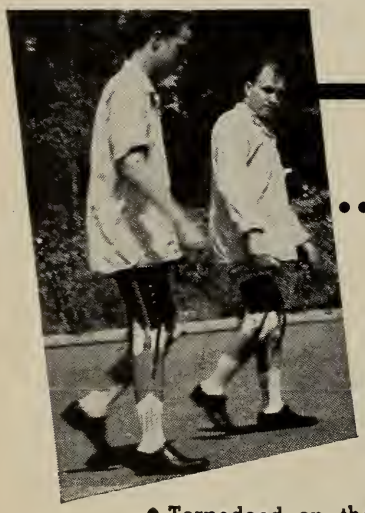
Stages of the process by which, in human beings, cancer cells are gradually derived from normal cells are not yet understood. However, the developmental stage of cancer may be described as "precancerous" in contrast to the stage in which cancer is capable of metastasis. Certain conditions, such as warts and moles, often become malignant and may be precancerous.

(Continued on Page 28)



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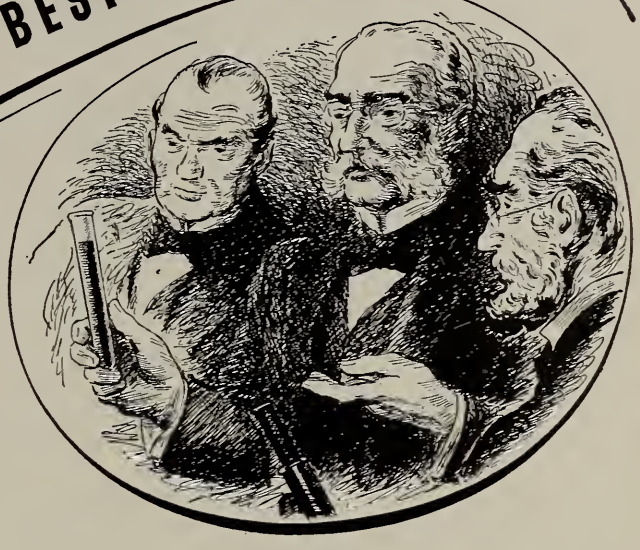
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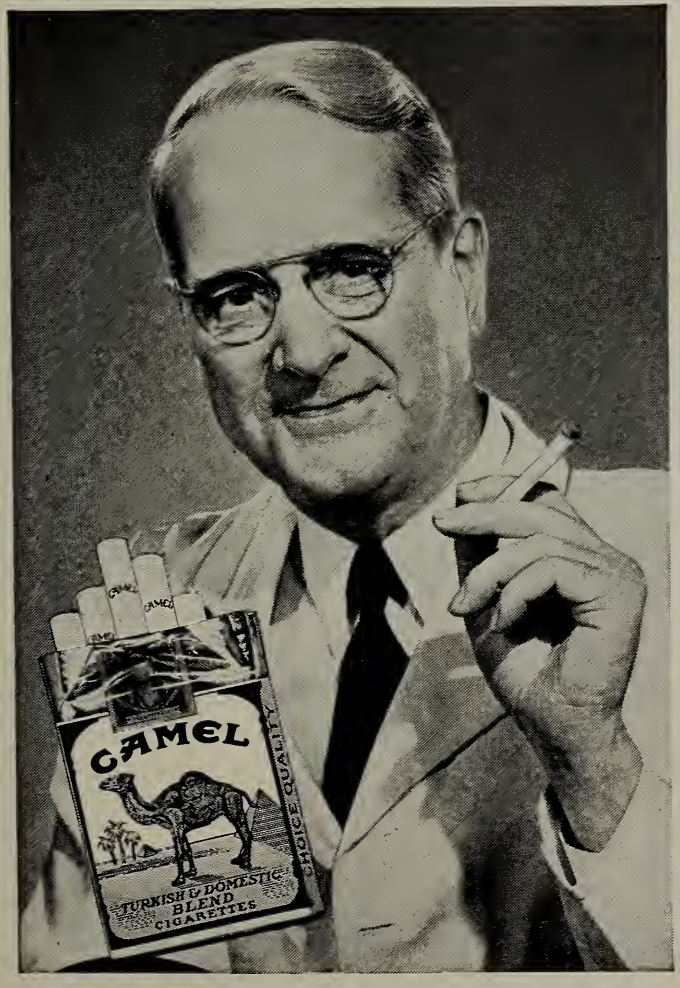


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TWO NEW PROCEDURES AID DIAGNOSIS OF CANCER

(Continued from Page 24)

In research, the step from embryonic tissue to cancer appears to be short, says Dr. Greene, adding: "If a crystal of methylcholanthrene or other so-called carcinogenic hydrocarbon is added to the embryonic organ at the time of transfer, a carcinoma characteristic of the transplanted tissue develops within 30 days."

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Rubinstein describes a study of 216 patients at the Montefiore Hospital from whom bone marrow was extracted by both the new procedure and the standard one of drawing marrow from the breast bone.

This new procedure is especially helpful in determining the spread of cancer to the bones. Often material from the hip bone contains cancerous cells when material from the breast bone does not, he says.

The presence of these cells in bone marrow may be the first positive indication of cancer in a hidden location. Dr. Rubinstein found that bone marrow indicated such cancer when x-ray films failed to do so. The new procedure is easier, safer, and better suited for repeated use than the standard one, he says, and can be used to diagnose leukemia, multiple myeloma, anemia, Hodgkin's disease, cirrhosis of the liver, sprue, and kidney diseases.

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(Continued from Page 8)

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California MEDICINE

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BAL (2, 3-Dimercaptopropanol) in the Treatment of Massive Overdosage with Mapharsen

CHARLES D. ARMSTRONG, M.D., *Menlo Park*, WILLIAM J. FLEMING, M.D., *Durham, N. C.*, and WILLIAM G. THALMANN, Major M.C., *San Francisco*

BRITISH anti-lewisite, familiarly known as BAL, was developed during the last war as an antidote for the arsenical blister gases. Although distributed to troops principally in the form of ointment to be applied in case of conjunctival or cutaneous exposure, BAL has now been shown valuable in the treatment of systemic poisoning with arsenic, gold, mercury, cadmium, and lead. Most of these applications were suggested by the extensive studies carried on in Britain and in this country. Some of the information gained in these investigations has been released in the form of large symposia, the component parts of which concern the biochemistry,[3] toxicology, pharmacology and experimental therapeutics,[18] and clinical uses[17] of BAL.*

MODE OF ACTION OF BAL

Peters, Stocken, and Thompson[21] advanced the fundamental concept that agents which combine with and inactivate the sulfhydryl groups of the activating proteins of enzyme systems, will interfere with the activity of those systems. Thus the pyruvate oxidase system[25] was found to depend upon the SH groups for its activity, and trivalent arsenicals were found to attack particularly those enzymes responsible for carbohydrate and fat metabolism.[26] At first, thiamine[13] and para-aminobenzoic acid[24] were used in an attempt to stimulate the disabled cellular economy. More promising was the finding[25] that arsenic and other heavy metals could be "detoxified" by giving compounds (particularly those with sulfhydryl groups), whose thiol groups exerted a greater affinity for arsenic than that possessed by the attacked tissue thiols. Dithiol compounds particularly were able to form a relatively stable, non-toxic, ring form thioarsenate which appeared promptly in the urine.[3a] A simple aliphatic dithiol, 2, 3-dimercaptopropanol (BAL), some of the BAL glucosides, and certain of the monothiols were the most useful of some 44 mercaptans tested in this regard.[12] The reaction is thought to be abetted by the similar spacial relationships of the SH radicals in the antidote and in the tissue proteins from which the heavy metal is displaced.[26] The reaction of arsenic with BAL may be represented as:

$$\begin{matrix} CH_2SH \\ CHSH \\ CH_2OH \\ \text{BAL} \end{matrix} + RAsO \longrightarrow \begin{matrix} CH_2SH \\ CHS\ AsR \\ CH_2OH \\ \text{BAL—As Compound} \end{matrix} + HOH^2$$

It seems very probable that other heavy metals besides arsenic combine with tissue proteins to interfere with tissue respiration,[14] and also that they may be attracted from the tissue proteins by BAL with which they form excretable compounds. In this group may be included antimony, bismuth (although urinary excretion does not rise), chromium, mercury, nickel,[18g] cadmium,[18f] vanadium, lead, stibium, and zinc.[29]

CHARACTERISTICS AND TOXICITY OF BAL:

2, 3-dimercaptopropanol is a colorless liquid with the typical skunk-like odor of the mercaptans. It is soluble in oil with the aid of a solubilizing agent such as 20 per cent benzyl benzoate, but it may also be prepared in an ointment base for percutaneous administration. On the skin BAL is painful, may form wheals,[17e] and cutaneous sensitization has occurred.[26]

From the Medical Service, Letterman General Hospital.

The opinions expressed in this paper are those of the authors, and do not necessarily reflect the official opinion of the Medical Department of the United States Army.

*BAL in a 10 per cent solution in 20 per cent peanut oil is available commercially.

Intramuscular injection of the substance in oil is less disturbing, but is often followed by intense local pain and cellulitis.[12]

Unfortunately, BAL may itself be toxic to enzyme systems. With oxygen it destroys hemin or oxyhemoglobin, reacts instantly to form hemoglobin from methemoglobin, and keeps cytochrome C in a reduced state.[29] It may inhibit brain glycolysis and the action of insulin.[29] In animals, sufficient doses may produce tremors, convulsions, coma, collapse, and death. Metabolic acidosis occurs with a lowered blood pH and CO_2 combining power, an increased serum lactic acid and amino nitrogen. Blood sugar rises initially but falls to hypoglycemic levels before death, and liver glycogen is reduced.[18a]

It has been felt that the ready penetration of BAL into the cells[30] may accentuate its toxicity to tissue metabolism. Accordingly less diffusible glucosides of BAL have been used (BAL Intrav-9) to combine with arsenic which is free in the blood stream, which diffuses out of the cells, or which may be carried from the cells to the blood by a small nontoxic dose of BAL itself.[9]

Doses of BAL less than 3 mg. per kg. of body weight produce mild reactions in about 14 per cent of cases[12] when administration occurs every four hours. Four-hourly doses of 5 mg. per kg. will cause symptoms in about 50 per cent of cases; a single dose of 8 mg. per kg. results in a marked reaction. Cumulative toxic effects which are absent with three-hourly administration of 5 mg. per kg. appear when that dose of the drug is given every two hours.[17c]

Characteristic symptoms, aside from local pain and cellulitis, are transient. They include: variable elevation of the systolic and diastolic blood pressures, most marked 45-120 minutes after injection, usually returning to normal within two hours; peripheral vasoconstriction with small doses or vascular collapse with large doses; nausea and vomiting; a burning sensation of the lips, mouth, throat, and eyes, sometimes with accompanying rhinorrhea, lacrimation, and salivation; sweating of the forehead and hands; burning and tingling of the extremities; pain in the teeth; general muscular aches; and constriction in the chest and a feeling of anxiety and agitation. The symptoms usually reach a maximum 10 to 30 minutes after injection and subside completely in the succeeding 20 to 50 minutes.[12]

Barbiturates have been suggested to diminish these effects,[26] as has epinephrine subcutaneously, or ephedrine sulphate (25 to 50 mg.) half an hour before the injection of BAL.[27]

THERAPEUTIC USES OF BAL

The dosage of BAL depends somewhat upon the metal causing the poisoning and the type and severity of the intoxication. In the treatment of acute gold toxicity (including thrombocytopenia and agranulocytosis,[19] 200 mg. of BAL given intramuscularly every four to six hours for ten doses has given good results; while 50 to 100 mg. twice daily for two to four days may relieve dermatitis.[10] It is interesting that arthritic symptoms may return following BAL-displacement of gold from its connection with the tissue sulfhydryl groups.[22] Soluble, slowly absorbed forms of gold may be more readily displaced.[10]

Mercury poisoning has been successfully treated in 25 of 26 cases by large doses of BAL: 5 mg. per kg. of body weight initially, followed by 2.5 mg. per kg. in two to four hours, and a third dose of the same size within the first 12 hours.[8,17f] Treatment of this type begun within four hours of the poisoning will save patients who ingest up to 1.5 gm. mercuric chloride.[17f]

Because of its frequency, arsenic poisoning, and particularly poisoning with the therapeutic arsenicals, has become one of the great fields of BAL usefulness. Several series of cases[1,7,11,12,15] have been reported. Eagle[11,12] from the available evidence in his large series of cases has arrived at the following schedule of BAL dosage in arsenical poisoning: in severe complications (exfoliative dermatitis, encephalitis, blood dyscrasia, jaundice, massive overdose) —3 mg. per kg. of body weight every four hours for the first two days; every six hours for the third day, and twice daily thereafter for ten days, or until recovery is evident; in mild complications (dermatitis, fever)—2.5 mg. per kg. body weight every six hours for the first two days, twice daily for the third day, and once or twice daily for the next ten or twelve days. Somewhat larger doses may be required for patients exposed to arsenical blister gas. It seems wise to err on the side of overdosage with BAL; inadequate or delayed treatment must be avoided.

With such administration of BAL, urinary excretion of arsenic rises to a peak about two hours after each injection. In some cases it may be seen to decline gradually for 4-7 days as BAL is continued. In jaundiced patients, results of excretion studies are more equivocal.[12]

In Eagle's series,[11,12] BAL therapy was associated with complete recovery of 44 of 55 patients with toxic encephalitis due to arsenic; of 10 of 11 patients with agranulocytosis; of every patient among 44 with arsenical fever; and of none of three with aplastic anemia. In 88 cases of arsenical dermatitis (51 of these exfoliative) BAL usually stopped the progression of the dermatitis and encouraged healing. Of 14 patients with jaundice (in whom needle-borne virus hepatitis must be considered), five showed prompt, and two debatable response to BAL treatment.

Of therapeutic interest is the observation that trypanosomes and spirochetes inactivated by arsenic are resuscitated by BAL.[17a]

CASE REPORTS

We have recently observed the dramatic benefits of BAL in two patients, each of whom received, through inadvertance, the contents of a ten-dose ampule of mapharsen. The injections were given at close intervals. The mistake was immediately recognized, and we were called in consultation. BAL treatment was begun within 30 minutes, an intramuscular injection of 3 mg. BAL per kg. body weight being given as the initial dose. This dose was repeated

every four hours for the first two days, every six hours for the third day, and twice daily for eight days thereafter, and once upon the twelfth and last day of treatment.

Urinary arsenic excretion levels were determined by the molybdenum blue method[16] every two hours during the first 24 hours, and subsequently upon aliquot parts of a 24 hour specimen. (See charts.)

In view of the usual effects of arsenic upon the skin,[17b,26] blood,[5,12,15,23] kidneys,[1] liver,[4,5,12,23] heart,[13] and central nervous system,[4,5,12] the patients' daily follow-up included: a physical examination, a complete hemogram, urinalysis, serum creatinine, thymol turbidity test, cephalin cholesterol flocculation test, Van den Bergh test, and electrocardiogram. The spinal fluid was examined twice. Bromsulfalein retention and blood cholesterol levels were determined periodically in each patient. Observations were repeated when the patients were completely asymptomatic, six weeks after the overdose of mapharsen. The results of all examinations were within normal limits, with the exception of those findings noted in the following reports.

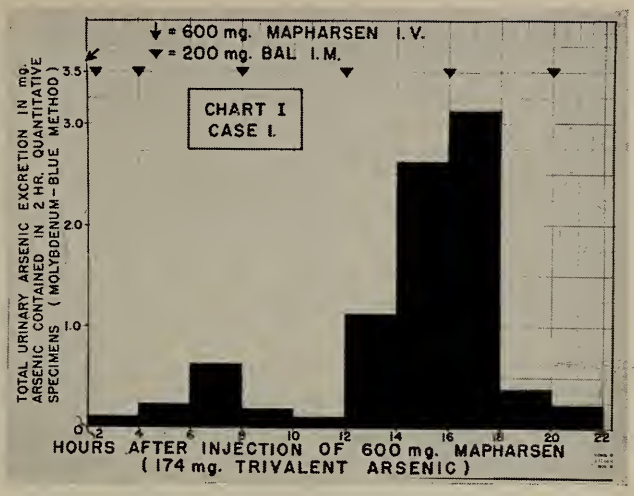


Chart 1.—Case 1: Arsenic Excretion in Urine, First day of BAL treatment.

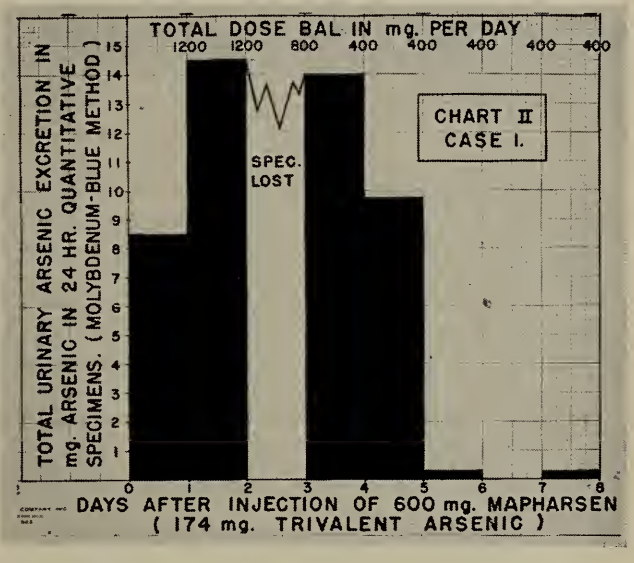


Chart 2.—Case 1: Arsenic Excretion in Urine, First week of BAL treatment.

Case 1.—The patient, a 30-year-old man, entered Letterman General Hospital on 11 July 1947 for treatment of asymptomatic neurosyphilis. A diagnosis of secondary syphilis had been made in March, 1946, and the patient was given 2,400,000 units of penicillin. At that time the spinal fluid, which contained 109 cells, was Wassermann negative. In August, 1946, the spinal fluid was Wassermann positive in all dilutions, with no pleocytosis. The patient received 10,000,000 units of penicillin intramuscularly between 31 October and 16 November 1946, and had 25 hours of therapeutic malarial fever above 104° F. between 1 November and 9 November 1946. The reactions to Wassermann and Kahn tests of the blood remained positive. On 18 July 1947 the spinal fluid Wassermann was still positive but results of Wassermann and Kahn tests of blood had become negative. It was decided to reinstitute treatment with penicillin, heavy metals, and typhoid induced pyrexia.

On 2 August 1947, the patient was inadvertently given 600 mg. of mapharsen (containing 174 mg. of trivalent arsenic). Nausea, vomiting, and some epigastric pain immediately followed the injection. BAL therapy was begun 30 minutes after the injection. The patient continued to feel nauseated, to vomit on occasion (the vomitus contained 1.2 mgm. of arsenic on analysis), and to have a loose, watery diarrhea without gross blood. He was, however, able to retain oral fluid and food, and, after the first 36 hours, became nauseated only following the injection of BAL.

Since completion of treatment, the patient has been entirely asymptomatic except for a slight scaly exfoliation of the skin of the hands and feet still noticed on 23 October 1947. Association between the BAL injection and arsenic excretion in the urine is noted in the accompanying charts 1 and 2. Serially repeated laboratory observations have revealed the following deviations from normal: Immediately following arsenic injection, the blood showed 4,000 leukocytes per cu. mm., of which 45 per cent were neutrophiles. On the second day, leukocytes had risen to 15,000 per cu. mm. with 78 per cent neutrophiles. The urine remained protein-free. Thymol turbidity test values rose to an abnormal level. A day after the injection the total Van den Bergh was 3 mgm. per 100 cc. but rapidly fell to normal limits. Six weeks following the last arsenic injection, the only abnormal laboratory finding was a persistently positive cephalin flocculation test of 3 plus. The patient has received no medication except BAL since 2 August 1947.

Case 2.—A 31-year-old Negro soldier entered Letterman General Hospital on 28 July 1947 with the diagnosis of rheumatic pericarditis. In January and again in April, 1947, at another hospital, he had had several episodes of precordial pain on exertion, and was found to have electrocardiographic changes which were interpreted as indicative of pericarditis. At the time of entry into this hospital, the patient was entirely asymptomatic and physical examination was not remarkable, except for a soft blowing, apical systolic murmur. Serial electrocardiograms and review of previous electrocardiograms were reported to show changes characteristic of sub-acute pericarditis, the cause of which was never determined. Primary syphilis was treated in 1945 with an unknown amount of penicillin, arsenic and bismuth. On entry into this hospital, results of all laboratory examinations were within normal limits, except for positive reactions to Kahn and Wassermann tests of the blood. On 9 May, 1947, the blood contained 80 Kahn units, but the Wassermann reaction was negative. At this hospital repeated Wassermann and Kahn reactions were doubtfully positive and anti-complementary, and the highest Kahn titer that could be obtained was 4 units. Cardiolipin reaction was positive. The spinal

fluid was repeatedly Wassermann negative. The syphilologist at this hospital considered this an instance of treatment failure, and advised anti-syphilis therapy to consist of 8,000,000 units of penicillin with concomitant mapharsen and bismuth.

Treatment was begun on the 25th of July, 1947. On the 2nd of August, the patient inadvertently was given 600 mgm. of marpharsen intravenously. Extreme nausea followed, and the patient complained of abdominal cramps, and vomited. (The vomitus contained 2.5 mg. arsenic on analysis.) BAL treatment was instituted 30 minutes after injection. The symptoms rapidly subsided, and except for a few loose, watery bowel movements without blood, the patient remained asymptomatic. No symptoms followed BAL injections. Urinary levels of arsenic with relation to the BAL therapy and pertinent laboratory data are shown in the accompanying charts. Serial complete blood studies, liver function tests and electrocardiograms did not reveal abnormalities. The patient remained entirely asymptomatic and six weeks following the arsenic injection, physical examination disclosed no abnormality. Results of all laboratory studies, including electrocardiograms, were also within normal limits. The Kahn titer remained 4 units. The cause of the patient's chest pain and abnormal electrocardiographic findings has not been determined.

COMMENT

In both of the cases presented the patients received a massive overdose of marpharsen and were promptly treated with BAL. Neither patient developed striking signs of BAL toxicity or the visceral toxic effects usually attributed to arsenic poisoning. The transient bilirubinemia and persistently positive reaction to the cephalin cholesterol flocculation test seen in Case 1 are of doubtful significance. The urinary excretion of arsenic during the BAL treatment of these patients is summarized in Table 1.

BAL TREATMENT OF MASSIVE OVERDOSAGE WITH MAPHARSEN

Massive overdosage with the therapeutic arsenicals is distressingly common.[4,5,6,12,23,26] Particularly frequent is the accidental administration of the contents of a ten-dose mapharsen vial (600 mg. of mapharsen or 174 mg. of arsenic). The ordinary result

Table 1.—*Urinary Excretion of Arsenic on BAL Treatment*

	Case 1	Case 2
Trivalent Arsenic Injected	174.0 mg.	174.0 mg.
At the end of first 12 hours:		
Total BAL injected	600 mg.	750 mg.
Urinary Arsenic:		
Total excr. in mg.	8.7 mg.	12.4 mg.
Total excr. as per cent of injected Arsenic	5.0%	7.1%
At the end of second 12 hours:		
Total BAL injected	1200 mg.	1500 mg.
Urinary Arsenic:		
Total excr. in mg.	8.7 mg.	12.4 mg.
Total excr. as per cent of injected Arsenic	5.0%	7.1%
At the end of the fifth day:		
Total BAL injected	4000 mg.	5000 mg.
Urinary Arsenic:		
Total excr. in mg.	46.9 mg.	51.9 mg.
Total excr. as per cent of injected Arsenic	27.0%	30.0%

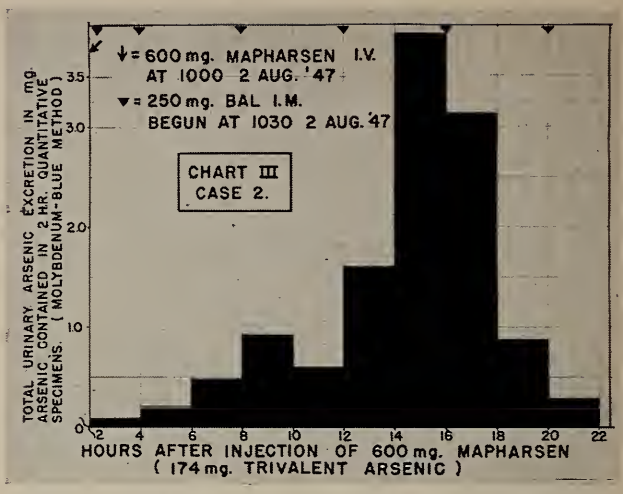


Chart 3.—Case 2: Arsenic Excretion in Urine, First day of BAL treatment.

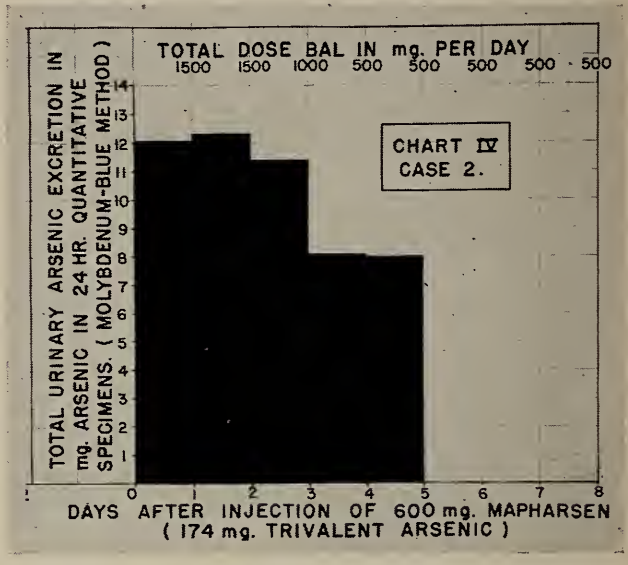


Chart 4.—Case 2: Arsenic Excretion in Urine, First week of BAL treatment.

in such cases before the advent of BAL is well represented by Rathmell's description[23] of the case of a man who rapidly developed marked hepatomegaly, jaundice, hematemesis, hematuria, albuminuria, and nitrogen retention, and died in coma 72 hours after the arsenical injection. Postmortem examination showed multiple petechial hemorrhages, acute hepatic necrosis, kidney necrosis, and a bone marrow condition said to be indistinguishable from that found in the nutritional anemias.

Following the introduction of BAL, such maladroitness has rarely led to death. Eagle[12] discusses the treatment of four patients who received 7 to 20 times the usual dose of arsenic. The first patient received 600 mg. of mapharsen and was treated with 2.6 mg. of BAL per kg. body weight within 30 minutes. The symptoms of poisoning disappeared within 30 minutes. The patient was given 1500 mg. of BAL during the next four days. Asymptomatic jaundice appeared on the second day; the icterus index was 65 units on the fourth day, and 30 units

on the sixth day. The patient recovered completely. Eighty mg. of arsenic, or almost half the dose received, was excreted in the urine within the first five days. The second patient was given only 400 mg. of mapharsen and recovered with 900 mg. of BAL given over six days. The third patient developed abdominal pain and clammy perspiration following 600 mg. of mapharsen. Adequate BAL therapy was begun in 24 hours, and recovery was complete. The fourth patient received 1200 mg. of mapharsen and was given only three injections of 150 mg. BAL. He died despite an initially favorable response.

CONCLUSIONS

BAL is effective in the control of heavy metal poisoning by virtue of its ability to displace the metals from the sulfhydryl groups of the tissues where their presence interferes with cellular metabolism. It must be remembered, parenthetically, that where the metal exerts a beneficial action, as with therapeutic amounts of gold and arsenic, this action may be lost when the sulfhydryl groups are freed. Despite its own features of toxicity, BAL may now be considered the treatment of choice in poisoning with gold, mercury, or arsenic. In massive arsenical overdosage, due most often to confusion of the one-dose and ten-dose mapharsen ampules, early and adequate treatment with BAL may be expected to save life and allow complete recovery. This is demonstrated by the two cases presented. Urinary arsenic excretion studies made in these two instances indicate a striking increase in arsenic excretions during the second 12 hours of BAL therapy (when about 1,000 mgm. of BAL has been given). The total arsenic excreted in the urine amounted to about 30 per cent of the arsenic which was injected.

SUMMARY

1. BAL (2, 3-dimercaptopropanol) is briefly discussed, its value in the treatment of heavy metal poisoning with gold, mercury, or arsenic is emphasized, and dosage schedules are reviewed.

2. Two cases are presented in which BAL therapy completely counteracted the effects of a 600 mg. dose of mapharsen. Data are presented on the urinary excretion of arsenic under the influence of BAL.

1111 University Drive, Menlo Park.

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Treatment of Duodenal Ulcer by Conservative Gastric Resection with Partial Vagotomy

ARNOLD STEVENS, M.D., *Los Angeles*

THE recent introduction by Dragstedt and his associates of complete double vagotomy in the treatment of peptic ulcer has been received with considerable enthusiasm. Although this is a worthy contribution, a word of caution is probably in order. Granted that complete vagotomy has so far seemed to effect a clinical cure in most cases of duodenal ulcer, there are certain theoretical and practical objections to the use of this procedure.

Theoretically, the vagus nerves are among the most important in the body. They constitute the parasympathetic nerve supply of a large portion of the abdominal viscera, including the stomach. So far as the stomach is concerned, a variable degree of cardiospasm, pylorospasm, and gastric atony should result from the complete severance of the vagus nerve fibers. Furthermore, vagus section alone does not attack the so-called hormonal factor in the secretion of gastric acid, which is proven by the response of vagotomized patients to histamine. Some observers have stated that this factor is unimportant. This viewpoint, however, is debatable. Lahey and others have effected a cure in certain cases of stomal ulcer following gastric resection, where it was necessary at the initial operation to leave a small portion of the pyloric antrum, by subsequently reoperating upon the patient and removing this portion of the stomach.

From a practical standpoint, disturbance of motility of the stomach has seemed to be the most important objection to the procedure. Most surgeons advocating vagotomy have stated that gastric retention following vagotomy is of a transient nature. In the experience of certain others, this has not consistently been the case. McIntyre, Kipen, and the writer, on the joint graduate teaching service of the University of Southern California, the College of Medical Evangelists, and the University of California at Los Angeles, have recently started to recheck vagotomized patients who were operated on approximately a year ago at the Veterans Hospital at Sawtelle. So far, ten patients have been called back for reexamination. The studies made on these patients include roentgenograms of the stomach following a standard barium meal. This has been completed on the ten patients. In five cases in which vagotomy alone was performed the emptying time of the stomach in one was normal. In the other four there was a 24-hour retention of barium of from 30 per cent to 85 per cent. One patient with 70 per cent retention had two small gastric ulcers demonstrated by roentgenographic and gastro-

Senior Consultant in Surgery, Veterans Hospital (Sawtelle). Associate Clinical Professor of Surgery, University of California at Los Angeles.

scopic examination. In the four cases vagotomy seems to have been complete, as indicated by the insulin tests made at this time. In all these cases the stomach had emptied in four hours or less before vagotomy.

In the remaining five cases, one patient, ten months after vagotomy for stomal ulcer had been done following gastric resection, showed some retention of barium at the end of ten hours, although the stomach was practically empty in six hours. In four cases supplementary gastroenterostomy had been done in conjunction with vagotomy, and in two of these the stomach was practically empty of barium in six hours while in the other two there was 75 per cent retention at the end of that time. All these patients had well placed posterior gastroenterostomies.

There is a current trend toward combining vagotomy with gastroenterostomy. There seem to be at least two objections to this procedure. In the first place, it is difficult to evaluate the results of a single procedure, as vagotomy, when combined with another procedure such as gastroenterostomy, particularly when this latter procedure alone appeared to afford excellent results in the treatment of duodenal ulcer for a great period of time. Many patients having gastroenterostomy seemed clinically cured for many years until stomal ulcers developed. The second theoretical objection to gastroenterostomy is that making a new opening in the stomach does not attack the basic cause of retention, namely, atony. In the studies at Sawtelle pylorospasm, cardiospasm, and diarrhea have not been important sequelae of vagotomy from a practical point of view. The investigations at the Veterans Hospital will include the recheck with barium of the emptying time of the stomach in all cases in which vagotomy, combined with gastroenterostomy, was done about a year previously. When the study is completed this year, it will be reported.

Complications such as hemorrhage, perforation, and complete obstruction from recurrent ulcers following vagotomy have resulted in death in a few cases, although not in sufficient number to condemn vagotomy.

Gastric resection, with the removal of three-fifths of the stomach and the ulcer-bearing portion of the duodenum, has stood the test of time probably as well as or better than any of the surgical procedures heretofore used in the treatment of duodenal ulcer. Although the results, on the whole, have been good, unpleasant complications, including stomal ulcer, occur. Fatalities sometimes result from the blowing out of the duodenal stumps. Experimental data apparently applicable to this procedure are somewhat confusing. James Watson, working in the laboratory of Frank Mann at the Institute of Experimental Medicine at Rochester, Minnesota, performed fundusectomies on dogs which included the removal of most of the acid-secreting cells of the stomach. Reductions in both free and total hydrochloric acid were noted immediately after operation on dogs in which extensive resection was done. In subsequent operations 15 to 18 weeks later, the acid curve was elevated and in six months reached a point practically as high as it was preoperatively. This work suggests that the removal of the acid-bearing glands of the stomach will not eradicate the acid factor in the production of ulcer. On the other hand, Priestley's work on animals in the same institution implies that removal of the hormonal factor in the pyloric portion of the stomach alone is not of major importance in the cure of ulcer. However, as mentioned before, stomal ulcers following exclusion operations where a portion of the pyloric antrum has been left intact have been cured by subsequently removing this remaining portion. This clinical observation is difficult to dispute.

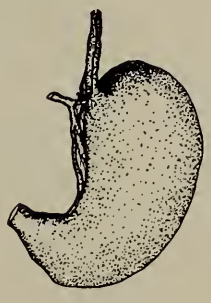


Figure 1

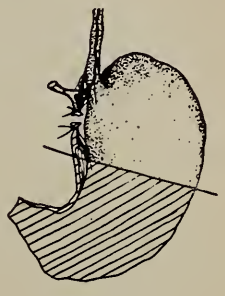


Figure 2

In an attempt to improve the results of radical gastric resection and to make the operation safer so far as leakage from the duodenal stump is concerned, Stevens, Sloan, and Danglade, a few years ago, began to utilize the combined procedures of conservative gastric resection and partial vagotomy. The purpose of this procedure is to attack both the hormonal and nervous phase of the secretion of gastric acid without the removal of the duodenal ulcer itself. It was believed unwise because of the importance of the vagus nerves, considering parasympathetic distribution, to divide both nerves completely. To use a simple hypothesis: If an electric light bulb is likely to burn out because of too strong a current, is it better to cut off the current entirely and substitute candlelight or to reduce the electric current to the point that the bulb gives a satisfactory light without burning out? The answer would seem to apply to complete and partial vagotomy.

Clinical and experimental studies, however, indicate that partial vagotomy alone will not effect a cure of duodenal ulcer. Granted that this is true, will a combination of this procedure and removal of the gastric hormonal element result in clinical cure of this lesion?

The answer may be supplied at some later date by follow-up studies of a series of patients which the author has treated by this method. In this series the vagus nerve fibers accumulating on the lesser curvature of the stomach were included in a mass ligation and division of the coronary artery high on the lesser curvature. (According to the anatomical dissections of Dragstedt, this should include at least 75 per cent of the fibers of both vagus nerves. (Figures 1 and 2) The procedure is simple and is not time-consuming.

Approximately one-half of the stomach, including the pyloric portion, was removed rather than the con-

TABLE 1.—*Results Following Complete Vagotomy*

Case	Pre-op Free HCL Clinical Units	Post-op Free HCL Clinical Units
1	24	12
2	44	15
3	40	0
4	60	20
5	85	5
6	30	20
7	35	20
8	47	0
9	50	0
10	25	5
Average	44%	9.7%

TABLE 2.—*Results Following Combined Partial Vagotomy and Conservative Gastric Resection*

Case	Pre-op Free HCL Clinical Units	Post-op Free HCL Clinical Units
1	45	0
2	38	0
3	60	0
4	68	0
5	53	0
6	36	0
7	14	6
8	32	8
9	32	12
10	60	0
Average	43.8%	2.6%

ventional three-fifths of the stomach. (Since it is difficult, at best, for the surgeon to determine exactly what proportion of the stomach he is removing, if doubt exists, a larger rather than a smaller amount should be removed.) Experience has shown that removal of less than one-half of the stomach results in the frequent occurrence of stomal ulcer. Removal of half of the stomach eliminates part of the acid glands and a large part of the chemical phase of the secretion of gastric acid. The so-called hormonal factor is not entirely eliminated, however, as has been indicated by postoperative studies with histamine. The postoperative reduction of gastric acid, following this relatively conservative combination of procedures, is more consistent than that following complete double vagotomy alone. This is illustrated by Charts 1 and 2. The data on the ten cases shown in Chart 2 are typical of the series as a whole. Insulin tests which have been made recently showed a reduction of free hydrochloric acid from an average of 69 per cent preoperatively to an average of 17 per cent postoperatively. This suggests that partial vagotomy as executed in this series is effective.

As previously stated by Stevens, Sloan and Danglade, it is not necessary to include removal of the duodenal ulcer with gastric resection to cure the lesion. On the other hand, the poor results with exclusion operations show that it is necessary to remove all of the pars pylorica. In our series the indications for operation were largely obstruction and repeated hemorrhage. Approximately 40 per cent of the cases were in the latter group. There has been no recurrence to date, and in none of the cases was the ulcer removed. In our series the stomach was divided at or just below the gastroduodenal junction. Rather than dissect the posterior wall of the duodenum, which heals poorly, from the head of the pancreas, the capsule of the pancreas, which heals rapidly, was used as a reinforcing layer in the closure of the duodenal stump. Some surgeons have objected to this method because of what they consider likely morbidity from leakage of the duodenal stump even though they grant it is not necessary to remove the ulcer. In our series, however, there has not been a single incidence of leakage.

It is planned to report, in detail, the postoperative results in this series of cases five years after the one-hundredth operation. To those using this procedure, results so far seem better than with other procedures they have tried. This is merely a preliminary report, however, and no deductions are justified at this time. It is hoped that those so inclined will use the method of conservative gastric resection and partial vagotomy, as described herein as a check on this study.

Probably most surgeons whose results have been good with conventional gastric resection should continue to utilize the procedure until time has proven other methods to be superior. This excepts the cases with stomal ulcer following high gastric resection for which complete vagotomy is probably the treatment of choice. By the same token, it seems reasonable that those interested and experienced in the problem of vagotomy should continue with this important study. As Berne has aptly stated, the present status of vagotomy is that of an uncompleted experiment.

120 Lasky Drive, Beverly Hills.

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Orthostatic Hypotension and Orthostatic Tachycardia

New Clinical Observations, Successful Treatment with Paredrine, and Review of Literature

Anton S. Yuskis, M.D., *San Diego*, and George C. Griffith, M.D., *Pasadena*

Bradbury and Eggleston[4] in 1925 first described orthostatic hypotension and since then relatively few reports have been recorded in the literature. Orthostatic hypotension is characterized chiefly by a sudden, sharp decrease in blood pressure when the afflicted patient assumes the upright position; and when the blood pressure reaches a low level, weakness and syncope result. The characteristic signs and symptoms are faintness, weakness, dimness of vision, severe headache, arrhythmias and syncope. When the patient assumes the erect position, especially after arising in the morning, or after exertion or fatigue, deficient perspiration, localized or generalized, and impaired renal function or oliguria may occur. Intolerance to heat, especially during the summer, impotence, and a positive reaction to the Flack[11] test are usually present. The blood pressure when the patient is supine is usually normal but in the standing position the systolic blood pressure may fall below 50-60 mm. of mercury. Faintness, dizziness, or syncope may follow. If a patient has exhaustion in the morning which decreases during the day, or dimness of vision or syncope which occurs on assumption of the erect position and disappears when supine, or if there are episodes of diminished sweating or of syncope inadequately explained, orthostatic hypotension should be suspected. The occurrence of orthostatic tachycardia with orthostatic hypotension has been often observed.

This condition has been considered by some to be the result of failure of adequate constriction of arterioles or a defect in the function of the sympathetic nervous system when the patient stands. Many observers[3, 6, 24] have emphasized the relationship between orthostatic hypotension and disease of the nervous system. Others[2, 5, 9, 15, 19, 20, 23, 26, 27, 31] have confirmed these observations and interpretations and have also advanced the possibility of the essential lesion in the hypothalamic region subserving the autonomic functions. Still others[1, 25] have emphasized the syndrome on the basis of disease of the peripheral autonomic nerves. It has been demonstrated repeatedly that this syndrome may occur in cases in which no disease of the nervous system could be discovered by clinical means.

From the Department of Internal Medicine, Cardiology, Graduate Division, University of Southern California School of Medicine and the Medical Service of the Los Angeles County General Hospital.

The paredrine used was made available by the Smith, Kline and French Laboratories, Philadelphia.

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Other studies[7, 10, 11, 14, 21, 22, 28, 30] have suggested that the defect in postural adaptation is not a defect in arteriolar vasoconstriction but rather one in maintenance of adequate return of venous blood to the heart and that this is an essential factor in the production of orthostatic hypotension and orthostatic tachycardia[7, 10, 11, 14, 21, 22, 28, 30]. Failure of venous return produces a marked decrease of the filling of the heart, decreased cardiac output, and, subsequently, diminution of the peripheral pulse.

MacLean, Allen and Magath[22] stress the point that a considerable amount of work has been focused on the nervous influences on the arterial side of the vascular system while the role of the autonomic nervous system in the maintenance of capillary-venous tone has been neglected. They[22] have classified this syndrome into two groups: Group 1—inconsistent orthostatic failure of venous return; group 2—consistent orthostatic failure of venous return. Under group 1 are classified those patients who may or may not demonstrate at any one time the classical signs and symptoms of failure of venous return in the erect posture, namely, weakness, faintness, and occasional syncope, associated with orthostatic hypotension or tachycardia. Both the signs and symptoms disappear in the recumbent position. Usually, no objective evidence of organic dysfunction of the autonomic nervous system can be demonstrated. Group 2 is composed of those patients in whom objective disorders of the autonomic nervous system are common. These patients are those who are suffering from tabes dorsalis, diabetic neuritis, combined sclerosis of pernicious anemia, exophthalmic goitre, diabetes insipidus, disseminated sclerosis, hypopituitarism with chromophobe adenoma, syringomyelia, Adie's syndrome, myosthenia gravis, Addison's disease, and sprue. To this group belong, also, those patients who have undergone extensive sympathectomy for hypertension and who have a consistent orthostatic defect of venous return for a variable period after operation.

Minor grades of circulatory disturbances may be seen in effort syndrome and convalescence following infectious diseases.

The treatment of orthostatic hypotension has consisted of various mechanical procedures such as tight abdominal and leg binders and the "head-up" sleeping position, the avoidance of any type of strenuous exertion on warm days and the use of various vasoconstrictors as well as an increased oral intake of salt and small doses of desoxycorticosterone[5, 6, 7, 8, 12, 13, 15, 17, 18, 27]. Efforts to find a satisfactory remedy for orthostatic hypotension have been disappointing.

PLATE I





BEFORE TREATMENT



AFTER TREATMENT

PLATE II





BEFORE TREATMENT



AFTER TREATMENT

PLATE III





BEFORE TREATMENT



AFTER TREATMENT

PLATE IV





BEFORE TREATMENT



AFTER TREATMENT

This is especially true of sympathomimetic or vasoconstricting drugs. Usually the dosage of paredrine used had been small and the beneficial results only temporary.

Since wide variations of blood pressure, heart rate and symptoms may occur, a study of patients who have orthostatic hypotension requires careful control with regard to external temperature, hydration of the body, and the intervals between feedings. Clinical observations under controlled conditions are presented on four patients who had marked, consistent defects of venous return. The effect of the postural state on the vascular pattern of the retinal vessels and the cardiac rhythm is demonstrated. The effect on the venous return by a single large oral dose of paredrine is shown. The treatment has been symptomatic and no claim to a cure is made.

CASE REPORT

The following case report demonstrates the effect of posture on the retinal vascular pattern, venous pressure, and circulation time:

A white man, diabetic, aged 23 years, entered the Los Angeles County General Hospital on August 20, 1946, complaining of diarrhea, numbness of his lower extremities, impotence, marked weakness, dizziness, severe headache with blurring of vision and occasionally syncope which occurred after getting out of bed in the morning. The patient stated that he had to lie down to obtain relief, that his symptoms were much worse in the morning and that he progressively improved as the day advanced. The patient perspired lightly over his face and neck and was intolerant to heat.

Pallor and a dry, scaly skin were noted in the general physical examination of the patient, who appeared much younger than his stated age. The brachial blood pressure in the supine position was 105 mm. of mercury systolic and 75 mm. diastolic, and the pulse rate was 86. When the patient had been erect for one minute the systolic blood pressure had dropped to 80 mm., the diastolic blood pressure to 68 mm., the pulse rate had increased to 96 and he began to complain of weakness, dizziness, headache and blurring of vision. After two minutes of standing the blood pressure was 30 mm. systolic and 0 diastolic, and the pulse rate 120; and before the pulse rate could be taken again, the impulses became very feeble and rapid and the patient collapsed. After the patient had been in bed in a supine position for one minute, almost all the symptoms disappeared.

The carotid sinus syndrome was absent and there was no clinical evidence of Addison's disease. Pulse rate and blood pressure readings are summarized in Table 1.

The venous pressures and the circulation times as determined by using 20 per cent sodium decholin, studied in the various positions are shown in Table 2.

The retinae were studied to determine if changes in the vascular pattern occurred with changes in posture. Interesting changes, not previously described, were observed and these observations are shown in Table 3 and in the colored plates made from paintings of the fundi.

Ephedrine was given at first in treating the orthostatic hypotension, but no improvement was noted. Paredrine was administered in doses of 20 to 60 mgm. four times a day without much effect. Since the symptoms occurred immediately after the patient arose in the morning, it was decided to use a large single dose of paredrine, orally, 30 to 60 minutes before he got out of bed. Paredrine was administered in single doses as high as 200 mgm. without any undesirable reactions, and a dose of 160 mgm. was finally found to be effective. After the administration of paredrine the patient did not complain of marked weakness, severe headache, dizziness or blurring of vision and syncope did not occur. The patient was then able to be up and about for the remainder of the day.

Before treatment with paredrine, the blood pressure would drop to about 30 mm. of mercury systolic and 0 diastolic, whereas after the use of paredrine the lowest recording was 70 mm. systolic and 40 mm. diastolic. Other effects noted are shown in Table 4.

Course: This patient took 160 mgm. of paredrine, daily, in a single dose, orally, for four and one-half months with complete relief of symptoms and without toxic effects. It was impossible to follow him for a longer period, as he moved away from this area.

Table 1

Position	Blood Pressure	Pulse
Supine	105/75	84
Supine with legs elevated	120/80	80
Supine at 30° angle	90/50	94
Standing:		
1 min.	88/68	96
2 min.	30/ 0	110
3 min.	0/ 0	120 to?

Table 2

Position	Circulation Time Arm-Tongue in Seconds	Venous Pressure MM. Water
Supine	18	0°—65
Supine with legs elevated	12	
Supine at 30° angle	20	45°—78
Standing	26	90°—88

Table 3.—*Retinal Vascular Patterns*

Position	Blood Pressure	Pulse	Before Treatment	After Treatment
Supine	110/60	84	Normal.	Normal.
Supine with legs elevated	120/80	80	Increased redness disc and fundus, marked distention and tortuosity of veins and less streaking of arteries.	Slight to moderate distention veins. No apparent change noted in arteries.
Supine at 30° angle	90/50	94	Slight pallor of disc, smaller veins.	No apparent change.
Standing	50/20 30/0	96-120	Marked pallor of disc and fundus, veins empty before arteries, both arteries and veins are narrow and faintly visible.	Slight pallor of disc and fundus. Arteries and veins well filled and clearly visible.

TABLE 4—*Blood Pressure*

Position	Treatment Before	After
Supine	105/75	110/80
Supine with legs elevated	120/80	116/80
Supine at 30° angle	90/50	110/80
Standing	30/ 0	80/60-90/65
Pulse		
Supine	86	84
Supine with legs elevated	82	88
Supine at 30° angle	94	86
Standing	120	90

CASE REPORT

The following case is similar to the first one and demonstrates the effect of posture upon the retinal vascular pattern and the effective control of venous return with paredrine:

A woman, aged 37, complained of dizziness, blurred vision, weakness, headache and faintness of two years' duration. The carotid sinus syndrome was absent and general physical examination disclosed no abnormality. The brachial blood pressure in the supine position was 108 mm. of mercury systolic, 80 mm. diastolic, and the pulse rate was 72. In the supine position with the legs elevated the blood pressure was 128 systolic, 78 diastolic and the pulse rate 80. With the patient in the erect position, at the end of two minutes the blood pressure was 80 systolic, 58 diastolic, the pulse rate 100 and the patient became very weak, dizzy and almost collapsed. The effects of posture upon the vascular pattern of the retina were similar to those observed in the first case described. Paredrine, orally, in a single daily dose of 100 mgm. 45 minutes before arising has controlled this patient's symptoms.

CASE REPORT

The following report illustrates a typical case of orthostatic hypotension in which effective control was not obtained with the administration of divided doses of paredrine but was achieved after a large single dose was administered:

A man, aged 55 years, complained of dizziness, weakness, dimness of vision and headache of several years' duration. The carotid sinus syndrome was absent. No abnormality was noted upon general physical examination. The blood pressure in the supine position was 110 mm. of mercury systolic, 76 mm. diastolic, and the pulse rate was 76. With the patient in the supine position with the legs elevated, the blood pressure was 122 mm. systolic, 80 mm. diastolic, and the pulse rate was 80. With the patient in the erect position, after three minutes of standing, the blood pressure was 84 mm. systolic, 60 mm. diastolic and the pulse rate 100. Paredrine, 40 mgm. three times a day and then every four hours, did not improve the patient's condition but when it was given in a single daily dose of 100 mgm. orally, 30 minutes before the patient arose, the symptoms were controlled effectively.

CASE REPORT

The following report of a typical case of orthostatic hypotension demonstrates the effect of posture on cardiac rhythm. This observation has not been previously described:

A physician, aged 52 years, had known that he had orthostatic hypotension with the usual symptoms and a postural cardiac arrhythmia for many years. The carotid sinus syndrome was absent and no abnormality was noted upon general physical examination. The blood pressure in the supine position was 104 mm. of mercury systolic and 70 mm. diastolic, and the pulse rate was 78. In the supine position with the legs elevated the blood pressure was 122 mm. systolic, 80 mm. diastolic, pulse rate 76. With the patient in the erect position, at the end of two minutes the blood pressure was 74 mm. systolic, 50 mm. diastolic, and the pulse rate 110. The electrocardiographic tracings (Figure 1) showed the onset and offset of arrhythmia due to the effect of posture. The tracings showed a change from normal sinus rhythm to premature contractions of auricular and ventricular origin to auricular fibrillation on assuming the erect position. The reverse was true when the patient assumed the supine position with the legs elevated. The blood pressure rose to normal (122 mm. systolic, 80 mm. diastolic) with a pulse rate of 76, and the arrhythmia reverted to normal sinus rhythm. Paredrine in a single daily dose of 140 to 160 mgm. taken orally one hour before arising in the morning controlled this patient's symptoms and arrhythmia.

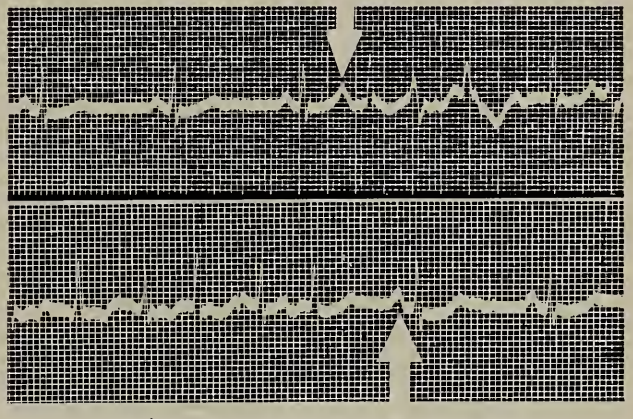


Figure 1. Above, Onset; Below, Offset.

COMMENT

It appears that the essential factor in the syndrome of orthostatic hypotension and orthostatic tachycardia is the failure of return of an adequate amount of venous blood to the heart. This defect of venous return becomes evident in a very short time after the patient stands; conversely, adequate circulation, a normal heart rate and blood pressure follow the resumption of a supine position.

The cause of this disorder appears to be generalized abnormally low venous capillary tone. In the syndrome of orthostatic hypotension, pooling of abnormal quantities of blood occurs caudad as the patient assumes the erect position and the elimination of this syndrome occurs when the pool of blood is shifted cephalad either with or without elevation of the lower extremities with the patient in the supine position. However, when the legs are elevated the syndrome is eliminated sooner. Because of this pooling of blood, with the patient in the erect position, failure of normal venous return occurs, resulting in anoxia with its signs and symptoms.

New clinical evidence to support this view is strongly suggested by the following observations:

1. With the patient in the supine position, elevation of the legs produces an increased hyperemia with distention and tortuosity of the retinal vessels, slight elevation in blood pressure, slight decrease in pulse rate and a shortened circulation time. When the legs are lowered, with the patient still in the supine

position, the retinal vessels become smaller in diameter, producing a decreased hyperemia of the retinae. With the patient in the upright position, the reverse occurs and the circulatory defect as seen in the retinae is marked and is characterized by pallor of the disc and fundus due to the decreased amount of blood in the retinal vessels with an associated drop in blood pressure, increased pulse rate and venous pressure and a prolonged circulation time. Resumption of the supine position abolishes these phenomena.

2. The effect upon the heart is shown by the abnormal cardiac rhythm and by the depression of the S-T segments in the electrocardiogram. The mechanism responsible for these changes is due to the decreased venous return to the heart and the resulting anoxia of the myocardium. Wiggers[29] states that pathological studies suggest that localized interference with the natural blood supply is one of the most common factors. Special regions of the nodal and conducting tissue are supplied with individual coronary artery branches, experimental ligation of which almost invariably leads to disturbances of conduction or rhythm. Katz[16] states that in electrocardiograms of a patient with orthostatic hypotension, there may be S-T-T changes on the patient's assuming the upright position and that these changes disappear if the standing posture is maintained. Such changes were not noted in patients observed by the author of this presentation.

The mechanism responsible for the maintenance of normal capillary venous tone or postural vascular adaptation is not fully understood. Because of the apparent absence of this tone, a sympathomimetic drug, without any central action, relatively non-toxic and safe in large doses, 100 to 200 mgm., orally, was used at a time when it was most needed with the hope that it would increase, by its vasopressor effect, the capillary-venous tone, thereby increasing the venous return to the heart and would maintain this action in a manner approaching normal and long enough for the normal mechanism to take over. It is felt from the observations presented herein that these effects were obtained.

CONCLUSION

1. New observations in the vascular pattern of the retinae in the syndrome of orthostatic hypotension and orthostatic tachycardia are reported for the first time.

2. New observations of cardiac arrhythmia, myocardial ischemia and injury in the electrocardiographic pattern in orthostatic hypotension are reported for the first time.

3. Further clinical observations are reported as evidence that possibly the cause for this syndrome is generalized abnormally low venous-capillary tone in the body.

4. Paredrine is a safe sympathomimetic drug and should be administered in an amount sufficient to produce the desired pharmacological and physiological effects.

5. In four cases orthostatic hypotension and orthostatic tachycardia were successfully treated with a single, daily, oral dose of paredrine hydrobromide.

Note: Since this paper was prepared eight more patients with orthostatic hypotension have been studied with similar findings and results, but none of the patients showed cardiac arrhythmia or ischemia.

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Bronchial Asthma in Infants and Children—Its Diagnosis and Treatment

ALBERT H. ROWE, M.D., and ALBERT ROWE, JR., M.D., *Oakland*

BRONCHIAL asthma in early and late childhood as in adult life[3] and old age[4] is practically always due to food or inhalant allergy or both, rarely to drug and bacterial allergy. This conclusion is based on the demonstrated causes in 156 infants and young children up to the age of five years and in 255 older children up to the age of 15 years observed between 1940 and 1946, in whom good or excellent results have been obtained. These results compare with those in similar age groups published in 1937.[10]

In this series, asthma occurred twice as frequently in males as in females (Table 1), whereas in later age groups the males and females were equal in number. There was a familial predisposition to asthma in 50 per cent of the cases with a lesser tendency to other manifestations of allergy. As noted in Table 2, moderate or moderately severe symptoms of asthma were most common. The frequency of other manifestations of allergy is also shown, perennial nasal allergy occurring in 56 per cent.

TABLE 1.—*Number of Patients, Males and Females, and Family History of Possible Allergy*

	Age of Child 0-5 Years	5-15 Years	Totals
Number of Patients	156	255	411
Males	102	174	276
Females	54	81	135
Family History:			
Bronchial Asthma	84	125	209
Nasal Allergy	68	67	135
Headaches	14	28	42
Eczema	9	16	25
Hives	8	10	18
Gastrointestinal Symptoms	8	20	28

DETERMINATION OF ALLERGIC CAUSES OF BRONCHIAL ASTHMA

I. HISTORY

The history is more important than skin testing. This is recorded in all our patients according to a previously published plan.[5,8]

A. Evidence Indicating Food Allergy

1. Bronchial asthma due to food allergy may begin at any time of life, even in old age.

TABLE 2.—*Duration and Degree of Bronchial Asthma and Occurrence of Other Manifestations of Allergy*

Duration of Asthma (in years):	Age of Child 0-5 Years (156 Cases)	5-15 Years (255 Cases)	Totals
0- 1	73	35	108
1- 2	52	29	81
2- 5	31	77	108
5-10		98	98
10-15		16	16
Degree of Asthma:			
Mild	20	15	35
Moderate	43	79	122
Severe	76	130	206
Very Severe	17	31	48
Other Manifestations:			
Nasal Allergy			
(a) Perennial	92	165	257
(b) Spring to Winter	8	25	33
Hives	21	22	43
Eczema	71	84	155
Headaches	3	13	16
Gastrointestinal Symptoms	16	41	57

TABLE 3.—*Frequency of Asthmatic Attacks, "Colds" Before Attacks, Perennial Bronchial Asthma and Dietary and Environmental Histories Suggestive of Allergy*

	Age of Child		
	0-5 Years (156 Cases)	5-15 Years (255 Cases)	Totals
Regular Recurring Attacks	57	90	147
Irregular Attacks	92	109	201
"Colds" Before Attacks	78	84	162
Perennial Symptoms	83	176	259
Positive Dietary History	85	117	202
Positive Environmental History	17	106	123

Food allergy as the major or sole cause of bronchial asthma in infants and children is usually indicated by the following classical history. The asthma usually arises in the first three years, especially from the 16th to the 26th month. At times it is preceded by infantile eczema. The attacks usually recur regularly every two to eight weeks (See Table 3). Coryza, nasal congestion and sneezing due to nasal allergy rather than to an infectious cold, may precede the bronchial asthma by four to 24 hours, or may arise and continue through the attack. The asthma is characterized by varying degrees of dyspnea, wheezing and coughing, or coughing and wheezing may predominate. Fever often occurs, varying from 100° F. to 104° F., for one to four days. In the authors' opinion, the fever usually is due to food allergy,[10,11] although respiratory infection may be the major or secondary cause. Anorexia, nausea and, at times, vomiting occur during the attacks. The asthma may disappear rapidly, or wheezing, tightness in the chest and coughing may gradually decline in from three to ten days.

These attacks can be explained by the gradual accumulation of reacting bodies in the cells of the lungs. When they exceed the reacting threshold, they unite with the causative food allergens in the pulmonary and other body cells. With the exhaustion of these reacting bodies, the symptoms disappear, even though causative foods continue to be eaten. At regular intervals thereafter the reacting bodies redevelop and the attack recurs.

Between attacks, relief may be complete or partial. In a year or more this refractoriness may decrease with resultant intervening, even daily coughing, wheezing, tightness in the chest and dyspnea especially with exercise, after retiring and often from 2 to 5 a.m.

The attacks may only occur or be exaggerated from early fall to late spring, especially from December to April (See Table 3), and may be absent or decreased in severity and frequency during the summer months due to seasonal influences on food allergy[6]. When this summer effect is absent, perennial symptoms arise from food allergy.

It is also important to realize that most recurrent head "colds" (See Table 3), with or without bronchial symptoms, which recur at quite regular intervals every two to eight weeks are due to nasal and bronchial allergy, especially to foods, rather than to respiratory infection. Slight wheezing and tightness in the chest may be present, but definite bronchial asthma usually is absent. Fever, if present, also may be due to food allergy, though a secondary respiratory infection may be responsible. These "colds" usually recur from early fall to late spring due to the intensification of food allergy during these seasons, invaliding or keeping children in bed or out of school one-fourth to one-half of the time.

2. A dietary history of dislikes or disagreements for specific foods also suggests food allergy (See Table 3). Such a history is not indicative of clinical food allergy in all cases and often is negative when food allergy is responsible (compare Tables 3 and 4). Questions should be specific; for example: "Do you drink milk?" "Do you eat eggs?" "If not, why?" Allergy to foods, such as cottonseed oil or shortening, wheat or even pepper, which are combined with other foods is difficult to discover in a history, and must be recognized rarely through skin testing and usually through diet trial.

3. The authors have obtained limited help from detailed diet diaries, which usually are time-consuming to patient and doctor and rarely are accurate.

B. Evidence in the History of Inhalant Allergy

Inhalant in contrast to food allergy infrequently causes cyclic recurrent attacks with intervening refractoriness and freedom from symptoms. Occasionally encountered inhalants will produce irregularly recurring attacks. Usually the continued inspiration of inhalants causes persistent asthma, the degree of which may vary with the amount in the air.

Since pollens are in the air of most of California throughout the year except during the rainy season, perennial asthma of varying degrees may be due to pollen allergy alone. Asthma from dusts, animal emanations and other miscellaneous inhalants encountered indoors may occur or be exaggerated in the fall to spring months.

A detailed environmental history may or may not reveal possible causes. Inhalants in the home, from trees and other vegetations out of doors, and in working environments, especially in barns, animal yards and gardens, must be listed and suspected. Mold allergy must be considered in damp areas or home, especially where mildew and molds readily grow.[2]

When inhalant and food allergies are operative in the same patient, perennial asthma is usual. The symptoms may vary in degree according to the amount of the allergenic inhalants, especially pollens, which are inspired, the degree of allergy present, the allergenic foods ingested and the seasonal and geographic effects on food allergy.

II. SKIN TESTING

Skin testing should be done by the scratch tests with all important ingested foods and inhaled allergens. Intradermal tests with foods are not done by the authors because of the many reactions which are nonspecific or indicative of past or potential

allergy and because of the rare deaths[8,10] reported from such tests. When suspected inhalant allergy is not revealed by the scratch test or empiric desensitization with suspected inhalants is not helpful, then intradermal testing with 1-1000 dilutions of inhalants which have elicited no reaction in the scratch test may be done, especially in older children. The frequency of reactions in these infants and children (See Table 4) approximates that in adults[3] and old age.[4]

The fallibility of the skin test in demonstrating clinical food allergy must be remembered. Many of the small reactions to inhalants and especially to foods are nonspecific or indicate a past or potential allergy. This is true to a lesser extent of the larger reactions. Negative reactions, moreover, usually occur to most foods causing chronic or cumulative symptoms, as already noted, and to about 10 to 15 per cent of inhalants.

The clinical importance of positive reactions can be determined only by the reproduction of the symptoms with inhalation or ingestion of specific allergens by the symptom-free patient. The cumulative effect of food allergens especially may allow a food to be eaten for several days before symptoms arise. Moreover, temporary desensitization or refractoriness due to the seasonal allergenic effects may allow foods to be eaten for weeks before symptoms recur.

III. Elimination Diet for the Study and Control of Food Allergy

Since the skin test often fails to reveal clinical food allergy, one of the authors for over 20 years has used standardized elimination diets[8] for the study of possible food allergy. Because of the frequency of allergy in bronchial asthma to one of or all the cereal grains in addition to milk, egg, fish, nuts and less often other foods that are excluded from these diets, the cereal-free elimination diet is utilized. This diet, modified for infants, substitutes soy for animal milks and adds the proper vitamins, starches, meats, vegetables and fruits as age increases. A modified diet for children up to the age of three years is published,[8] and the cereal-free elimination diet for adults is available for older children.[8]

The advantages of the standardized elimination diets reside in the list of specific foods, the detailed menus with specific amounts of foods, the protection of weight and nutrition, the tested recipes for bakery products, the use of vitamins and calcium which harmonize with the diets, the ease with which the diets

Table 4.—*Number and Degree of Skin Reactions to the Scratch Test*

Pollens:	Age of Child 0-5 Years (156 Cases)	5-15 Years (255 Cases)	Totals (411 Cases)		Per Cent of All Patients
(a) Grass:					
0 – 1 +	35	79	114		
1 – 4 +	23	48	71	190	46%
4 + up	0	5	5		
(b) Fall:					
0 – 1 +	20	57	77		
1 – 4 +	9	20	29	106	26%
4 + up	0	0	0		
(c) Trees:					
0 – 1 +	21	57	78		
1 – 4 +	4	21	25	103	25%
4 + up	0	0	0		
(d) Cultivated Flowers:					
0 – 1 +	23	37	60		
1 – 4 +	2	14	16	76	18.5%
4 + up	0	0	0		
Animal Emanations:					
0 – 1 +	33	88	121		
1 – 4 +	8	24	32	158	38%
4 + up	1	4	5		
Miscellaneous Inhalants:					
0 – 1 +	21	61	82		
1 – 4 +	6	12	18	102	25%
4 + up	1	1	2		
House Dust:					
0 – 1 +	13	56	69		
1 – 4 +	2	11	13	84	20%
4 + up	1	1	2		
Fungi:					
0 – 1 +	3	6	9		
1 – 4 +	2	3	5	14	3%
4 + up	(Tests were not routine)				
Foods:					
0 – 1 +	50	60	110		
1 – 4 +	24	23	47	164	40%
4 + up	3	4	7		
No Reactions	38	46	84		20%

can be ordered in the hospitals and with which the office patient can be instructed in their use.

The elimination diets when accurately prepared insure proper weight, nutrition and growth. This is important since formerly eaten foods remain in the body for several days and possibly for a few weeks, necessitating the use of the diet for more than a few days.

The original diet should be continued until the period of relief is at least twice as long as preceding periods of relief. If prolonged daily symptoms have been present and relief arises in a few days to two weeks, continuing for an equal period, it is probable that the causative foods have been excluded from the diet. If attacks of asthma have recurred every two to six weeks, then relief must continue for four to twelve weeks, or longer, before this conclusion is justified. When chronic asthma has been present, the resultant cellular changes may not disappear until the shock tissues have been free from the allergenic foods for several weeks—and at times certain irreversible changes remain.

If persistent asthma is not relieved in one to three weeks or if recurrent attacks continue with the use of the diet, changes in the elimination diet as discussed elsewhere[8] may be indicated along with the study of possible inhalant, drug and (rarely) bacterial allergy.

When relief is assured, individual foods may be added, one every three to seven days, as advised in other publications[8]. Foods tolerated during the summer may cause symptoms in the fall to spring months due to the exaggeration of food allergy in those months.[6]

IV. STUDY AND CONTROL OF INHALANT ALLERGY

When the history indicates pollen allergy, even with negative skin reactions, desensitization is required. Our experience indicates the advisability of treatment with most of the pollens present in the air when the asthma occurs. Such multiple antigens contain from 5 to 30 pollens for each pollen season. Treatment is started with very weak dilutions, varying from 1-5,000,000 to 1-500,000,000,000 or even weaker dilutions for infants. The initial and at times desensitizing dose may be determined by serial intradermal titrations as advised recently by Rinkel. The doses are gradually increased, as tolerated, to successively stronger dilutions. In general the maximum dose during the first year should be as small as will give relief, rarely being greater than the 1-5,000,000 in infants and the 1-50,000 or 1-5,000 in young children. In adolescence the 1-500 or the 1-50 dilution may be tolerated and beneficial, especially in the winter and pre-seasonal periods. If symptoms recur during the season, the dose must be reduced at times to the very weak dilutions, which often are necessary for the control of atopic dermatitis.[9]

Pollen filters in the bedrooms and living rooms are helpful when pollen allergy is severe.

Fungus allergy must be studied in the patients suspected of inhalant allergy, especially if molds are found in damp rooms, closets or basements. Desensitization with antigens containing the prevalent fungi in the indoor or outdoor air or with autogenous fungus antigens may be necessary. Allergy to dust, animal emanations and miscellaneous inhalant allergens requires strict environmental control and desensitization with those allergens which cannot be eliminated from the inspired air. The dilutions and doses are similar to those advised for pollen therapy.

V. THE STUDY AND CONTROL OF BACTERIAL ALLERGY

Bacterial allergy as a major cause of bronchial asthma was not demonstrated in any case in this series. Tonsils and adenoids often had been removed without relief. In the authors' opinion, the so-called head "colds" which occurred for one or more days before the attacks of bronchial asthma in 162 of the cases as shown in Table 3 were due to the same food and, less often, inhalant allergens which were responsible for the subsequent or accompanying bronchial asthma or allergic bronchitis. As one of us has reported[11] for several years, the fever even up to 105° F. during these attacks also may be due to food allergy, though an associated respiratory infection must be ruled out. This is in contrast to Cooke's opinion[1] that such colds and fever favor bacterial allergy as a cause of so-called infective asthma. The leukocytosis in varying degrees and frequencies in these patients, as shown in Table 5, was usually due to food and/or inhalant allergies, since the control of these allergies resulted in normal values in practically all cases. Against bacterial allergy, moreover, was the occurrence of head colds or bronchitis actually due to infection without the development of bronchial asthma when the causative food and/or inhalant allergies were controlled. Mothers often state that "for the first time a 'cold' has occurred without any asthma."

Though bacterial allergy did not cause the bronchial asthma and the less frequent nasal allergy in these cases, a low resistance to respiratory infection seemed apparent in some patients. When this was probable, stock respiratory vaccine was administered, starting with a dose of 40,000 to 400,000 bacteria according to age, with a gradual subsequent increase, the injections being given every five to ten days until a dose of 20,000,000 to 120,000,000 was given as tolerated and according to age. The repetition of this final dose every seven to ten days throughout the fall, winter and spring months, or

TABLE 5.—*Leukocytosis in 411 Infants and Children With Bronchial Asthma Due to Food and/or Inhalant and (Very Rarely) to Bacterial Allergy*

	Age of Child			
	0-5 Years (156 Cases)		5-15 Years (255 Cases)	
Leukocytosis				
10–12,000	27		30	
12–15,000	20	63 (40%)	26	65 (25.5%)
15–20,000	14		9	
20–40,000	2		0	

even throughout the year, raises resistance in a specific or nonspecific manner and may also be of nonspecific benefit to the atopic allergy.

VI. PHYSICAL EXAMINATION AND ROUTINE LABORATORY STUDIES

Careful physical examination, all indicated laboratory studies on blood, urine and sputum and roentgen examination of the chest and, when indicated, of the sinuses must be used to rule out other recognized causes of dyspnea, wheezing and cough and reveal any other disease.[10]

THE CAUSES OF BRONCHIAL ASTHMA IN 411 INFANTS AND CHILDREN UP TO THE AGE OF 15 YEARS WITH GOOD OR EXCELLENT RESULTS FROM TREATMENT

These results were obtained by the control of the various allergies as listed in Table 6. By excellent results we mean complete control or only occasional wheezing, especially if a slight break in the diet or undue exposure to causative inhalants occurs. By good results we mean relief from all symptoms except for moderate wheezing or slight coughing one or two times during the night or with exertion due to lapses in cooperation or failure to discover or control all allergenic causes. In all patients severe symptoms may occur when allergenic foods are reintroduced into the diet with or opposed to the physician's orders. Food allergy alone was responsible in 143 cases, pollen allergy alone in 24 cases and other inhalants alone in 26 cases. Food allergy with or without inhalant allergy required control in 339 cases and inhalant allergies of all types with or without food allergy in 270 cases. Fungus allergy associated with other inhalant allergies was important in six cases. Evidence of minor bacterial allergy was obtained in five cases. A similar importance of the above causes has been demonstrated in the authors' patients in adult life and also in old age.[3,4]

Cooperation in these cases lasted from six months to six years.

INFANTS AND CHILDREN UNDER THE AGE OF 15 YEARS WHO WERE UNRELIEVED OF BRONCHIAL ASTHMA

From 1940 to 1946, 61 additional patients were seen. As shown in Table 7, 31 did not report after the first visit, 17 reported only during the first month, and ten from six to twelve months. Cooperation was satisfactory in only seven of these 61 patients.

TREATMENT OF MODERATE BRONCHIAL ASTHMA

The plan of treatment used by the writers to obtain good or excellent results in 411 infants and children is summarized under specific and symptomatic control.

A. Specific Control

1. When inhalant or drug allergies are not the sole obvious causes, food allergy is studied immediately with our standardized cereal-free elimination diet.[8]

2. When inhalant allergies of any type are indicated by history or skin testing, environmental control and, if necessary, desensitization with suspected allergens which the patient continues to inhale are necessary.

3. Rare bacterial and drug allergies need study as already discussed.

B. Symptomatic Control

This is necessary until the specific control reduces or eliminates the symptoms.

1. Ephedrine in doses of 4.0 mg. to 25.0 mg., according to age, every four hours often relieves or eliminates moderate symptoms. Phenobarbital in doses of 2.5 mg. to 8.0 mg. or corresponding doses of other barbitals may be given with the ephedrine to reduce resultant nervousness.

2. Aminophyllin by mouth in doses of 30 mg. to 90 mg., according to age, every three to twelve

TABLE 7.—*Unrelieved Bronchial Asthma in 61 Patients, Aged 0–15 Years, Seen from 1940 to 1946*

Number of Patients	61
Good Cooperation	7
Poor Cooperation	54
Time of Treatment:	
None	31
1– 4 Weeks	17
1– 3 Months	1
3– 6 Months	2
6–12 Months	10

TABLE 6.—*Causes of Bronchial Asthma in 411 Infants and Children as Determined By Good Results from Specific Control*

	Age of Child			Per Cent
	0-5 Years (156 Cases)	5-15 Years (255 Cases)	Total (411 Cases)	of 411 Patients
Food With or Without Other Allergies	138	201	339	82%
Food Allergy Alone	78	65	143	35%
Inhalant and Other Allergies	90	180	270	66%
Inhalant Allergies (Other than Pollen)	11	15	26	6%
Pollen and Other Allergies	79	165	244	59%
Pollen Allergy Alone	4	20	24	6%
Animal Emanation and Other Allergies	10	16	26	6%
Miscellaneous Inhalant and Other Allergies	8	14	22	5%
House Dust and Other Allergies	15	49	64	16%
Fungus and Other Allergies	2	4	6	1%
Bacterial and Other Allergies	2	3	5	1%
Excellent Results	83	146	229	53%
Good Results	73	109	182	47%

hours may relieve moderate asthma. Enteric coated tablets delay its action.

3. Potassium or sodium iodide in doses of one to ten drops in water three times a day often helps patients with persistent asthma. If swelling of submaxillary glands, blocking of the nose, headache or later a skin eruption occurs from allergy to iodine, it should be stopped. Later, smaller doses may be tolerated with benefit.

4. Epinephrine 1-100 by inhalation usually helps moderate asthma.

5. Epinephrine 1-1000 subcutaneously in doses of 0.1 cc. to 0.5 cc., according to age, every two hours if necessary, usually relieves symptoms which do not respond to the foregoing measures.

6. Intramuscular epinephrine 1-500 in gelatine in doses of 0.1 cc. to 1.0 cc., according to age and weight, every six to twelve hours may yield prolonged relief. Peanut, cottonseed or even corn oil should only be injected when absence of allergy to these oils is assured.

7. When severe asthma is not relieved by the foregoing therapy, aminophyllin in doses of 0.09 gm. to 0.2 gm., according to age, injected by vein slowly over a three-minute period is indicated in children over the age of six years. Intramuscular injections in doses of 0.09 gm. to 0.2 gm., according to age, may be given every six to twelve hours.

8. No morphine, codein, demerol, paraldehyde, or barbitals other than the already indicated doses of phenobarbital should be given to any case of bronchial asthma. Depression of respiration or cerebration with resultant anoxemia and at times death justify this rule.[10]

9. Other measures used in chronic cases as discussed elsewhere[8] may be advisable.

THE TREATMENT OF INTRACTABLE BRONCHIAL ASTHMA

The authors' treatment of intractable bronchial asthma is summarized under specific and symptomatic control.

The patients require hospitalization or a similar room and care at home. Immediate consideration of the probable major food and inhalant causes is imperative.

A. Specific Control

1. Unless inhalant allergy is the obvious sole cause, the cereal-free elimination diet is immediately ordered to study possible food allergy. If vomiting is present, intravenous glucose in saline or water as indicated by electrolyte balance is necessary. When nausea decreases, liquid or soft foods and later ordinarily cooked foods in the diet are given.

2. Inhalant allergy needs immediate study with strict environmental control. If pollen allergy is possible, a pollen window filter may be advisable in the pollen seasons. Desensitization, although it may be indicated, should be postponed until relief occurs.

3. Rare drug and less frequent bacterial allergies need study as already discussed.

B. Symptomatic Control

1. Epinephrine 1-1000 subcutaneously in doses of 0.1 cc. to 0.6 cc., according to reaction and age, every one to four hours may give relief.

2. If epinephrine does not help, aminophyllin by vein in doses of 0.06 to 0.3 gm., according to weight and age, given over a period of from three to five minutes every eight to twelve hours is advisable. This may also be given in 5 per cent glucose with or without saline.

3. With dehydration, especially with nausea or vomiting, intravenous 5 per cent glucose in saline or water according to sodium chloride and water requirements is necessary.

4. If asthma is extreme, especially if cyanosis or possible cardiac weakness is present, oxygen by tent or under pressure with BLB mask should be ordered. In the authors' practice, oxygen-helium has not been necessary in children. As a life-saving measure oxygen or oxygen-helium with Barach's positive pressure helmet may be of value.

5. The use of morphine, codein, barbitals, demoral or paraldehyde is contraindicated, especially in intractable bronchial asthma, for already discussed reasons.

6. As asthma decreases, the measures previously advised for the control of moderate symptoms become increasingly effective.

DISCUSSION

These good and excellent results in patients who gave proper cooperation demonstrate that food or inhalant allergies or both are responsible for bronchial asthma in infants and children as they are in mid-life and old age.[4] Food allergy was a sole cause in 50 per cent of infants and young children and it was associated with inhalant allergy in another 38 per cent of the cases. It was the sole cause in 26 per cent of the older group, being associated with inhalant allergy in another 53 per cent. Inhalant allergy of all types was a major or secondary cause in 58 per cent of the young group and 71 per cent of the older group of children. Thus food allergy is more important than inhalant allergy and is a more important sole cause in the younger children than in the older children. This demonstrated importance of food allergy is in marked contrast to the recent opinion of Hill.[12] Inhalant allergy, on the contrary, increases in the older children.

The usual inability to determine cumulative or chronic food allergy by skin testing is emphasized by this study. Skin reactions by the scratch test were obtained in approximately 40 per cent of all patients in whom food allergy was a cause of asthma. However, in practically all these patients some allergenic foods were not indicated by positive reactions and one or more positive reactions were not indicative of active clinical allergy. Moreover, no reactions to foods or inhalants occurred in 27 per cent of the young group or in 23 per cent of the older group, in most of whom food allergy was the sole cause.

Our frequent recognition of food allergy has been accomplished with the free use of the authors' cereal-free elimination diet[8] or its modifications. The advantages of trial diet of this type already have been noted. The usual failure of test-negative diets to demonstrate clinical food allergy has been discussed.

The classical history of bronchial allergy in children due to food allergy has been described for the first time in the literature. The regularity of the attacks due to refractoriness which arises to allergenic foods after an attack and the exaggeration or recurrence of bronchial asthma in the fall to spring months due to activation or exaggeration of food allergy during these seasons have been noted.

It is important to realize that most "head and bronchial colds" that recur regularly every two to eight weeks, especially from early fall to late spring, are also due to allergy, especially to foods, rather than to respiratory infection.

As discussed in this paper, the determination of inhalant allergy depends on history, skin testing and results of treatment. Most of the patients sensitive to inhalants gave positive reactions, although all positive reactions were not indicative of actual clinical allergy. As shown in Table 6, allergy to all types of inhalants is a slightly less important cause than is food allergy, and it increases in frequency in the older children.

Of these inhalants, pollens are much more frequent causes than are animal emanations, dust, fungi or miscellaneous inhalants. With Efron dust extracts during the last year, larger and more frequent reactions have been obtained, all of which are not of clinical significance. Pollen allergy, however, as a sole cause is rare compared with allergy to foods in these age groups.

In these infants and children bacterial allergy was not a major cause of bronchial asthma in any patient. No recovery depended on tonsillectomy and no nasal or sinal operations were performed. As already stated, the fever up to 104° F. which often occurs during severe attacks of asthma, usually is due to food allergy,[11] although associated respiratory infection, including pneumonitis, must always be suspected. The occurrence of infectious colds without the development of bronchial asthma when its causes are adequately controlled speaks against infection or bacterial allergy as a cause of the symptoms and fever.

Our plan of treatment thus immediately considers food and inhalant allergy as indicated by the history and skin testing. It also depends on the use of adrenalin hypodermically and on aminophyllin by vein in older children for the control of severe symptoms. For the control of moderate symptoms, ephedrine by mouth, epinephrine by inhalation, aminophyllin by mouth or by rectum and potassium iodide by mouth are usually effective. Morphine, other opium derivatives, demerol, paraldehyde and barbitals for relief of asthma are contraindicated in all cases for previously discussed reasons.

CASE REPORT

A boy 26 months old was first observed in October, 1944, because of bronchial asthma recurring since March every four to six weeks. Each attack had been initiated by exaggerated nasal symptoms lasting for one day, followed by wheezing, difficult breathing, coughing and fever up to 101° F. rectally for two days.

Since infancy, "head colds" had recurred every six to eight weeks, characterized by nasal congestion, blocking of the nose and sneezing, especially in the morning, and with a moderate fever. Mild nasal congestion and sneezing had continued between these colds. For the last eight months asthma had followed the colds.

Eczema involving the face had occurred between the ages of three months and nine months, and occasional hives had been present.

The dietary history revealed no dislikes or idiosyncrasies for any foods; drug and environmental histories were negative for allergy; family history revealed asthma in the maternal grandfather.

The physical examination showed a pale, slightly edematous nasal mucosa, slightly enlarged tonsils and diffuse evidences of bronchial asthma throughout both lungs. A roentgenogram of the chest showed no abnormality.

Results of urine analysis were normal. Blood examination showed hemoglobin 82 per cent, with leukocytes numbering 15,850 and erythrocytes 4,700,000. Differential: polymorphonuclear 52 per cent (nonsegmented 3 per cent), lymphocytes 34 per cent, large monocytes 1 per cent, eosinophiles 11 per cent, basophiles 1 per cent.

Skin testing with all important inhalants showed 1-plus reactions to chicken feathers, dog hair, glue, coastal sage, western ragweed and spearscale pollens. There were no reactions to skin tests with all important foods.

Treatment and Results: Because of the frequency with which food allergy causes regularly recurring head and bronchial "colds," with or without bronchial asthma, the authors' cereal-free elimination diet was prescribed. Calcium carbonate one-quarter teaspoonful in food two times a day and five drops of drisdol daily were ordered. In two weeks all nasal and bronchial symptoms had disappeared. Since Mull-Soy was refused, more prescribed meat was ordered to maintain protein requirements. Soy-potato bakery products made with the authors' recipes were eaten. The original diet was maintained for two months, after which additional vegetables and fruits gradually were added.

During the last one and a half years, corn, rye, oats, wheat, fish and recently egg and milk gradually have been added. No asthma has recurred, except on two occasions after the addition of rice—the first time in five days and the second time in nine days after its daily ingestion.

Two typical head colds have recurred with no resultant asthma. The child now sleeps quietly, has a good disposition, and gained eight pounds in one and a half years.

Discussion: The control of the recurrent head colds since infancy and of the more recent associated bronchial asthma with the elimination diet, demonstrates food allergy as the cause.

The addition of rice has caused asthma twice. If allergy to egg and milk originally were present, their long elimination from the diet could have raised tolerance so that they now produce no symptoms. If asthma recurs, especially in the fall, winter and spring months when food allergy so often is activated, the original cereal-free elimination diet will be resumed. Milk especially will be suspected.

No desensitization with inhalants and no injections of nonspecific agents or vaccines were given to yield this result.

CASE REPORT

A boy 3 years of age was first observed in May, 1944, because of bronchial asthma. Wheezing had developed six months previously on a ranch where there were many trees, animals and alfalfa. For one day preceding the beginning of the wheezing, a "head cold" characterized by coryza and sneezing had been present. Since then four similar increasingly severe attacks had occurred. Four of the five attacks had developed on the ranch and one in the patient's city home.

No other manifestations of allergy had occurred. No food dislikes or disagreements were elicited. The drug history revealed vomiting from a sulfa drug. Environmental history showed the presence of Bermuda grass in the lawn. No trees and no animals were around the city home. There was a family history of bronchial asthma in the maternal uncle, hay fever in the paternal grandmother and hives in the mother.

Upon physical examination, slightly enlarged tonsils were noted. No indications of asthma were ascertained since the patient was in a symptom-free period. A roentgenogram of the chest was normal, as were results of blood and urine analyses.

Skin testing by the scratch method with all important food and inhalant allergens showed 3-plus reactions to rice, oats, peas and navy beans, 2-plus to wheat, oats, tomatoes, stringbeans, peaches and prunes, and 1-plus to milk, eggs, potatoes, oranges and grapefruit. A 5-plus reaction to mugwort pollen was noted, 2-plus to alfalfa, cockleburr, spearscale and chrysanthemum pollens, 2-plus to kapok and cottonseed and 1-plus to tobacco and cat hair.

Treatment and Results: Because of the suspicion of pollen allergy, especially to alfalfa, as indicated by history and skin testing, desensitization with a multiple antigen containing all the important spring and summer and fall pollens in the areas in which the patient lived was started with the 1-50,000,000 dilution. The doses were increased so that by October the 1-5,000 dilution was tolerated. In the last one and a half years the 1-500 and later the 1-50 dilutions have been given at weekly intervals.

Although reactions were not obtained to animal emanations, other than cat hair, or to feed dusts, other than alfalfa, another antigen containing allergens of all the feeds and of all the animals on the ranch was administered along with the pollen antigen eight months after the first visit. An initial dose of 1-50,000,000 gradually was increased up to the 1-50 dilution at the end of one year.

Because of the positive skin reactions, especially to cereal grains, milk, egg and legumes, and the necessity of considering food allergy in all patients suffering from chronic recurrent bronchial asthma of the perennial type, the authors' cereal-free elimination diet minus peas and stringbeans was ordered at the first visit.

Severe asthma developed three days after treatment was started, and a mild attack occurred about two months later when the patient was at the ranch. His appetite increased in two weeks. In November the patient had a bad cold with no resultant asthma. Even though he has been in contact with alfalfa and has been on the ranch, no symptoms have occurred except for mild wheezing on one occasion when he was playing in the hay at the end of the first four months of treatment.

During the second year all foods gradually were added to the diet with no difficulty. In the fall of the third year a cough with fever up to 104° F. recurred on three occasions. Since reactivation of food allergy was suspected, the cereal-free elimination diet again was ordered. Since then all symptoms have been absent and a general diet gradually has been resumed.

Discussion: The results obtained with the antigens made of pollens, feed dusts and animal emanations indicate inhalant allergy as the major cause. Had larger reactions been obtained, treatment would have been started with a 1-5,000,000,000 or even a 1-500,000,000,000 dilution.

Despite the many positive skin reactions to various foods, the patient's history was not suggestive of food allergy. However, the possibility of food allergy was studied with the authors' cereal-free elimination diet minus peas and stringbeans. It is difficult to determine whether this diet aided in obtaining the good results in the first few months. The reappearance of the cough and fever in the fall and winter of 1946 does suggest temporary activation of food allergy, as often occurs in those months.

SUMMARY

1. Bronchial asthma in the authors' patients from birth to the age of 15 years is due principally to food allergy and, to a lesser degree, to inhalant allergy. Drug and bacterial allergies are rarely causative.

2. The classical history of bronchial asthma in infancy to childhood due to food allergy is described.

3. Recurrent head and/or bronchial colds with or without mild asthma every four to eight weeks, especially from September to May, are often due to chronic food allergy rather than to respiratory infections.

4. The fallibility of the skin test, especially in determining chronic food allergy, is stressed.

5. The use of standardized elimination diets is advised and the special value of the cereal-free diet is noted.

6. The use of environmental control and desensitization with inhalant allergens that cannot be avoided are available for the control of inhalant allergy.

7. The great rarity of bacterial allergy as the cause of bronchial allergy is stressed.

8. The specific and symptomatic treatment of chronic and intractable bronchial asthma is outlined.

2940 Summit Street.

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The "Pitfall" of Normal Results of Urinalysis

Donald W. Atcheson, M.D., *Riverside*

AS SYMPTOMS referable to genitourinary diseases are frequently vague and all too often do not follow the pattern commonly attributed to those diseases, the basic diagnostic study must be started with an open mind and the laboratory work confined to urine analysis and blood count. Occasionally when the urine analysis is reported as normal the tendency is to dismiss all possibility of urinary tract disease. This is a common "pitfall," and for that reason the following representative case histories are of interest. It will be well to note in the following reports the long duration and frequently the advanced state of the disease in the presence of normal urine.

CASE REPORTS

Case 1.—The patient, a woman aged 40, for eight years had had recurrent dysuria, frequency and pain in the area of the urethra upon voiding. There was no apparent reason for a fever of 99 to 100° F. which had not responded to penicillin. (The patient was sensitive to sulfonamides.) Examination revealed a blood pressure of 175 mm. of mercury systolic and 110 mm. diastolic. A moderately tender, smooth and movable mass was palpated in the right upper quadrant of the abdomen extending into the right loin. Urine analysis and cultures gave normal results upon several occasions. Cystoscopic examination and pyelograms revealed a moderately severe cystitis, right nephroptosis with ureteral kinking and early right hydronephrosis with definite decrease in function. Right nephropexy was performed and examination one year later revealed a decrease in hydronephrosis and the patient was free of all symptoms. Normal urine analysis findings previously had forestalled a complete study, with the result that the patient had been treated for cystitis alone.

Case 2.—A woman 29 years of age had been having episodes of left costovertebral angle pain, nausea, vomiting and fever for two years. There had been no dysuria, frequency, hematuria, gravel or other symptoms. Results of urine analysis usually were normal, but occasionally pus was found. Examination revealed temperature of 99.4° F. and tenderness in the left costovertebral angle but no other abnormalities. Cystoscopy and pyelograms disclosed bilateral hydronephrosis due to obstruction at the ureteropelvic junctions. Bilateral aberrant vessels were removed, bilateral nephropexies and pyeloureteroplasties were done, and the patient obtained complete relief of symptoms. Had the urine analysis not been repeated several times the relation of the symptoms to the urinary tract might have been missed.

Case 3.—A boy 17 years of age was referred for urological consultation because of episodes of left abdominal pain which had occurred every five to six months since childhood. They were frequently associated with left costovertebral angle pain, nausea and fever, but because of repeatedly normal results of urine examination, no genitourinary studies had been done. Examination revealed some tenderness in the left costovertebral angle and left side of the abdomen. Upon cystoscopy the bladder was found to be normal, but pyelograms revealed bilateral hydronephrosis with obstruction at the ureteropelvic areas and definite decrease in the function of each kidney. Both ureters were dilated to 10 (French) for several months but the symptoms continued, and eventually when an operation was performed, bilateral congenital ureteral fibromuscular strictures were found and pyeloureteroplasties were done. The patient was free of symptoms during several months of observation following the operation. Had undue importance not been ascribed to the normal results of urine analysis, the diagnosis and treatment might have been carried out earlier.

Case 4.—A 67-year-old man was referred with total gross hematuria. Results of urinalyses prior to this, however, had always been normal and there was no history of symptoms indicating genitourinary disease. Thorough studies revealed that the patient had a contracture of the bladder neck, a small fibrous obstructing prostate, a large diverticulum of the bladder, within which was a papillary carcinoma and a left hydronephrosis. All these conditions have been surgically corrected. This case is described to demonstrate that advanced genitourinary disease of long duration may cause no abnormality in results of urine analysis. The diverticulum had probably been steadily developing since childhood, the carcinoma for six to twelve months and the hydronephrosis for several months.

Case 5.—A woman, 48 years of age, had had vague left loin pain for many years, and once, 20 years before, had had gross hematuria. She was continually under medical care because of hypertension, and the urine, when analyzed from time to time, usually was found to contain albumin. Because it had never contained leukocytes or erythrocytes, no further studies of the kidneys were made until the patient had severe left renal colic. The pyelogram revealed a large left hydronephrosis. The diseased kidney was removed. Incidentally, the hypertension has been much less following the operation.

Case 6.—The patient, a woman 26 years of age, had been receiving dilatations of the right ureter in various cities for four years. The chief symptom was right costovertebral angle pain which was so severe that it had practically incapacitated her for the previous year. The patient also frequently had nausea, fever, dysuria and frequency, but results of urine analyses, which had shown the presence of infection the first three years, had been normal the last year. Examination proved the right costovertebral angle area to be tender. Cystoscopy showed a normal bladder. Pyelograms demonstrated bilateral bifid renal pelvices with the upper calyx on the right dilated and draining through a long narrow infundibulum. Heminephrectomy was attempted but because of technical difficulties it was necessary to do a nephrectomy. The patient since has had complete relief of symptoms and is now quite active and normal. This case is presented to demonstrate that longstanding incapacitating disease in the genitourinary tract may cause no abnormalities in the urine.

Case 7.—A 26-year-old woman complained of pain in the right side of the abdomen and loin. The temperature was 101° F. Six months before, laparotomy and appendectomy had been done for relief of the same symptoms, but no evidence of disease was found at that time. The symptoms subsided with bed rest. In complete urological studies, results of six urine analyses were normal, but pyelograms showed right hydronephrosis and a suggestion of an aberrant vessel. This was removed surgically and a nephropexy done, with relief of symptoms.

Case 8.—The patient, a woman aged 37, for several years had had recurrent episodes of dysuria, frequency, fatigue, nervousness and dull constant bilateral costovertebral angle pain. When physical examination revealed no abnormalities, and the results of several urine analyses were normal, the most apparent diagnosis seemed to be psychoneurosis. Urine cultures were done, however, and a growth of B. Aerogenes found. Pyelograms (Figure 1) show the extent of involvement. This case was one of polycystic disease of the kidney.

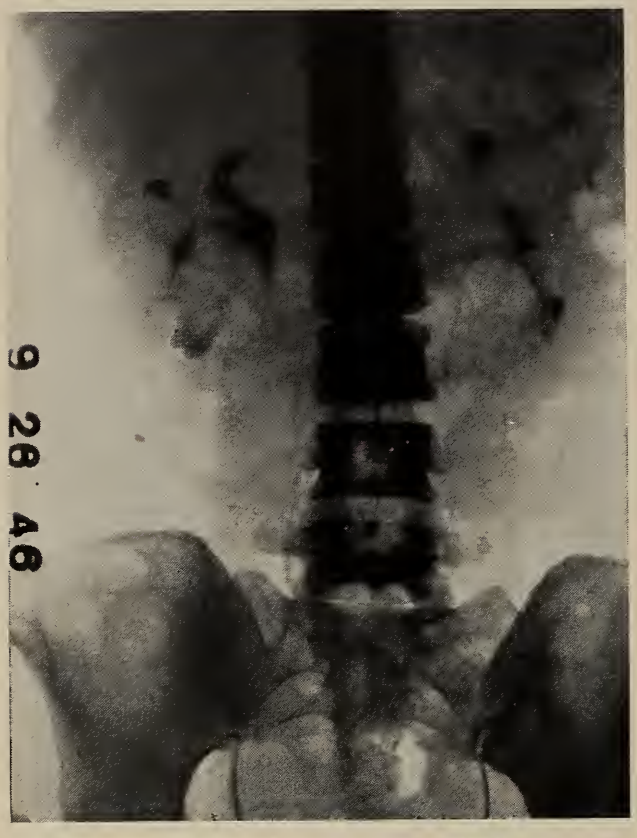


Figure 1.—Case 8: Polycystic disease.

Case 9.—The patient, a woman 53 years of age, complained chiefly of dull constant pain felt in the left buttock. Hysterectomy had been done six months before because of abdominal pain. There were no urinary symptoms of any sort and results of urine analysis were normal. Blood pressure was 176 mm. of mercury systolic and 106 mm. diastolic. There was a movable, heavy, non-tender mass in the left loin. At cystoscopy the bladder was found to be normal. Urine specimens from both kidneys were normal, and function was good bilaterally. However, pyelograms were suggestive of a tumor in the left kidney. A hypernephromatous kidney was removed.

In view of the minimal symptoms and the normal urine, the referring physician deserves much credit for obtaining complete urological studies so early. It is only by such early diagnosis that cures can be obtained in this condition. In approximately 70 per cent of cases, hypernephromata cause no abnormalities in the urine.

Case 10.—The patient, a girl ten years of age, had had an episode of rheumatic fever at the age of seven. At that time it was noticed there was a trace of albumin in the urine but because of the absence of pyuria and the dearth of symptoms suggesting urinary tract disease, the illness was considered as caused entirely by rheumatic fever and no further genitourinary studies were done. Although albuminuria continued for several years, it was still considered an aftermath of rheumatic fever until the family consulted another pediatrician and urological studies were obtained. Urine from the bladder and from the left kidney were found to be swarming with Gram negative bacilli, but urine from the right kidney was normal. The number of pus cells was always less than five per high power field. Pyelograms demonstrated left hydronephrosis and hydroureter with a stricture in the lower third of the left ureter. Treatment with chemotherapy and dilatation of the ureter have produced complete freedom from fever and other symptoms.

DISCUSSION

The ten cases presented, selected to demonstrate that obscure renal disease may occur at all ages in both sexes, illustrate that advanced urinary tract disease may exist and yet the urine be normal. For this reason it is wise to repeat urine analysis several times when the clinical picture is obscure and the diagnosis uncertain. When caring for a patient over a period of time it is often noticed that both erythrocytes and leukocytes appear in the urine in "showers" and that when these are washed away the urine is normal for a time. A specimen taken during a normal period would tend to throw one off the track.

In the preceding case histories it will be noted that in several instances the symptoms seemed typical of renal disease but inasmuch as results of urine analyses were normal, the logical diagnosis was set aside for a time and it was not until complete urological studies were made that the true state of affairs was found. All too often we treat the patients in such circumstances for recurrent cystitis and because of a reluctance on the part of the patient to undergo further examination or a feeling by the physician that the urinary symptoms are not disabling, no further study is made and it is not until considerable permanent damage is done to the urinary tract that the diagnosis is finally made.

The cases reported are not unusual. Included are cases in which the symptoms were caused by aberrant vessels, nephroptoses, intramural ureteral strictures, tumors, polycystic kidneys, hydrocalyces, diverticula of the bladder and carcinoma of the bladder. These are typical average genitourinary cases and represent a wide range of disease entities, yet all occurred in the presence of apparently normal urine.

For investigation of the urological tract no examination can take the place of cystoscopy and retrograde pyelograms. Intravenous pyelograms are useful but they leave much to be desired in demonstrating the bladder and ureters. They also frequently give a false sense of security concerning renal disease when the pelvis and calyces are not well filled. In difficult diagnostic problems it is not wise to "rule out" renal disease upon the basis of the usual intravenous pyelogram.

The cases reported illustrate once more the old precept that no single laboratory procedure is of as much value as a careful taking of history, physical examination and clinical impression. When these suggest kidney disease a normal result of urine analysis does not rule it out.

3768 Twelfth Street.

Massive Herniation of the Intervertebral Disc Producing Compression of the Cauda Equina

Howard A. Black, M.D., *Sacramento*

WRITINGS pertaining to massive herniation of the intervertebral disc, with compression of the cauda equina, have been submerged by the recent flood of literature on the more common unilateral disc syndrome implicating usually a single nerve root. Eleven cases of the condition under consideration have been gathered from the records of the neurosurgical services under the direction of Browder at the Kings County Hospital, the Long Island College Hospital and the Brooklyn Hospital, New York City. Analysis of the histories indicates there are certain features which aid in establishing a correct preoperative diagnosis. A composite history may be assembled which contains three stages in the progression of symptoms. Illustrative case histories will be presented.

The early literature relative to posterior herniations of the intervertebral structures contains many examples of massive herniation of a disc producing obstruction of the spinal subarachnoid space and compression of the cauda equina or of the spinal cord. In 1911 Goldthwait[5] postulated that dislocation of an intervertebral disc might cause compression of the cauda equina. He described a case which well may have been similar to the ones herein recorded. Middleton and Teacher,[6] in 1911, recorded the first verified case of extrusion of a large disc, secondary to trauma, with compression of the spinal cord. In 1916 Elsberg[3] stated, "I have seen one patient with a chondroma of the vertebra which caused symptoms from pressure on the cauda equina, and Oppenheim has described a similar case." It is known that the chondromas referred to in the literature then were in all likelihood what are now termed retroherniations of the intervertebral disc.

The first record of successful operation for the condition, with recognition of the nature of the offending agent, is that by Dandy.[2] In 1929, under the title of "Loose Cartilage from Intervertebral Disk Simulating Tumor of the Spinal Cord," he reported two cases in which the patients were successfully operated upon and stated, "The lesion is undoubtedly of traumatic origin." In 1930 Bucy[1] reported a similar case in which there was a partial block of the subarachnoid space on Queckenstedt test, and a complete block to lipiodol. Mixter and Barr,[7] in 1934, reported 19 cases, and in six of them the herniation was of the massive type producing obstruction of the spinal canal. Infrequently there have been other examples of the condition included in reports which directed attention primarily to the usual or unilateral extrusions. More recent literature includes the reports of French and Payne,[4] and of Ver Brugghen,[8] which deal with massive herniations of discs.

In the 11 cases studied it was observed that the histories of five patients presented three definite stages in the development of the syndrome, and the remaining histories differed only in omitting either of the first two stages. The following case illustrates the most commonly encountered history.

CASE REPORT

Case 1.—A chauffeur, aged 46, was admitted to the Brooklyn Hospital Jan. 2, 1943, complaining of pain in the legs and weakness and numbness of both legs. For the previous ten years he had had occasional attacks of pain in the lower part of the back. Eight months before admission pain radiated down the back of the left thigh and leg. Nine days before admission, while walking in his home, he coughed and suddenly was seized with lightning-like pain down the outside of both thighs followed by weakness and numbness of both legs and inability to urinate.

Examination disclosed marked weakness of all muscle groups of both legs. Achilles reflexes could not be elicited. The other deep reflexes were active. There was anesthesia in the second through the fifth sacral dermatomes bilaterally. The bladder was markedly distended and the external anal sphincter was lax. Roentgenograms of the lumbar spine showed no abnormality. The total protein content of the spinal fluid was 186 mg. per 100 cc.

At operation a large intervertebral disc, occluding the intraspinal canal, was found lying anterior to the dura at the fourth lumbar interspace, completely extruded from the intervertebral space. It was removed through an extradural approach. Later the dura was opened and the cauda equina found matted together at the level of the lesion.

Recovery from operation was prompt and at the time of discharge from the hospital the patient was considerably improved.

This case history may be summarized as follows: Intermittent attacks of pain in the lower part of the back for ten years, succeeded by pain radiating down the posterior aspect of one lower limb for eight months, and finally a sudden onset of symptoms suggesting severe compression of the cauda equina.

In the following case there was radicular pain suggestive of unilateral disc herniation, followed by symptoms of compression of the cauda equina; but there was no preceding stage of chronic backache.

CASE REPORT

Case 2.—A painter, aged 44 years, was admitted to the Kings County Hospital Aug. 17, 1942, complaining of paralysis of the legs. Three years previously there had been an attack of pain in the right buttock. The pain had spread down the back of the right thigh, and later down the leg, and usually was aggravated by coughing. Five days before admission to the hospital there was a sudden onset of pain

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in the legs accompanied by weakness of the legs, numbness of the buttocks, and inability to urinate.

Examination disclosed a moderate degree of weakness of the flexor and extensor muscles of the ankles and toes on both sides. Neither ankle jerk was obtained. The remaining deep reflexes were within normal limits. There was a marked degree of hypesthesia and hypalgesia in the region of the fifth lumbar through the fifth sacral dermatomes bilaterally. The bladder was distended one-half way to the umbilicus and the external anal sphincter was lax. Roentgenograms of the lumbar spine showed only scoliosis. The total protein content of the spinal fluid was 65 mg. per 100 cc. Roentgenograms taken in the sitting position after subarachnoid injection of lipiodol demonstrated a block at the fourth lumbar interspace.

At operation a large mass of white, fragmented, gristly material lay anterior to the dura at the level of the fourth intervertebral space, and almost completely occluded the intradural canal. The mass was removed and the wound closed in layers.

Recovery from operation was prompt and three weeks later, at the time of discharge from the hospital, the patient was able to walk unaided and to control the flow of urine moderately well. When last seen, three months after operation, he was able to walk a half mile without tiring and had normal control of the urinary bladder.

A third variation in the histories encountered in the group of 11 patients is illustrated by the following record, in which a period of backache was followed by sudden onset of symptoms suggesting compression of the cauda equina.

CASE REPORT

CASE 3.—A housewife, aged 52 years, was admitted to the Long Island College Hospital Feb. 14, 1934, complaining of pain in the lower part of the back and of inability to control the flow of urine. Two months previously a boring, cramping pain developed in the lower part of the back. Two weeks before admission to the hospital the patient was awakened at night by sudden, severe cramp-like pain which radiated down the backs of the thighs, and the following morning there was a feeling of numbness of the genitals and weakness of the legs.

The patient's gait was waddling and the left lower limb was favored, suggesting particular weakness of the muscles of the left calf although both ankles were weak. Neither ankle jerk was obtained but the other deep reflexes were active. There was hypesthesia and hypalgesia in the region of the second sacral dermatome on the right side. Roentgenograms of the lumbar spine showed no abnormality. The total protein content of the spinal fluid was 129 mg. per 100 cc.

Operation was refused and the patient left the hospital only to be readmitted a week later. Fluoroscopic examination after subarachnoid injection of a small amount of lipiodol disclosed a block at the fourth lumbar interspace.

At operation no epidural fat was present at the fourth lumbar level. When the dura was opened marked compression of the cauda equina was seen. The nerve roots were hyperemic. A transverse bulge of the anterior dural wall into the spinal canal was present at the level of the fourth interspace. The dura was incised and a large herniated disc removed.

Recovery proceeded well and at the time of discharge, 15 days later, the patient was free of pain, was walking, and had good control of the urinary bladder and bowels. Improvement continued and the ankle jerks returned.

The remaining records when analyzed are found to follow rather closely some one of the three patterns illustrated by the cases which have been presented. It will be seen that a composite history may be drawn from the group as a whole in which three stages in the advance of the symptoms are evident. The first phase is that of chronic backache. There is pain in the lower part of the back, usually intermittent, and often related to motion. The second phase is that usually associated with posterior herniation of a unilateral disc, with radiation of pain down the posterior aspect of one lower limb. The pain commonly is moderate or severe in degree, may be aggravated by coughing and sneezing, and may be associated with paresthesias. The third stage usually is distinctive, and consists of a relatively sudden onset of symptoms indicative of compression of the cauda equina—pain in both lower limbs, weakness of the legs, numbness of the legs and saddle area, and possibly paresthesias in the legs or saddle area, impotence, retention of urine, and trouble controlling the bowels. All three stages were noted in the histories of five patients; three patients gave histories indicative of stage one and stage three only; and three had only stages two and three, there having been no preceding period of chronic backache. Briefly stated, the composite picture is: Chronic backache for a variable period of time, followed by radiation of pain into one lower limb, and succeeded by relatively sudden onset of symptoms of compression of the cauda equina.

This symptom-complex most commonly is the result of one of three pathological processes: Massive herniation of a nucleus pulposus; collapse of a vertebra following invasion by tumor (usually carcinoma); or collapse of a vertebra weakened by infection (usually tuberculosis). When the neural compression is the result of vertebral collapse from tumor or tuberculosis, roentgen ray studies usually will demonstrate the pre-existing disease of the spine. When the compression of the cauda equina is secondary to carcinoma or tuberculosis, but there is no evidence of metastasis to the spine or tuberculous infection of the spine at the level of neural compression, the history frequently will indicate a relatively gradual progress of pressure. In such instances an epidural extension of the disease process may be the cause of the obstruction of the spinal canal.

Differentiation of the lesion under consideration from tumors of the cauda equina or of the conus medullaris or filum terminale appears possible when the history of the illness is analyzed. The third stage of the history—that of fulmination of symptoms, in which the patient, at the onset in relatively good health, rather suddenly becomes severely incapacitated—is seldom encountered in tumors. A correct diagnosis was made pre-operatively in ten of the eleven cases in this group of massive disc herniations.

There was a history of trauma to the back in only three of the eleven patients. Roentgenograms showed a narrowing of the involved interspace in only two patients in this series. A contrast medium was used to provide confirmatory evidence of localization in ten of the eleven patients. A complete spinal subarachnoid block (lipiodol was used in nine and

pantopaque in one) was demonstrated in eight instances, and in one case a nearly complete obstruction was present. One examination was technically unsatisfactory. The levels of the extruded discs were: The fifth lumbar interspace in three cases; the fourth lumbar interspace in seven cases; and the third lumbar interspace in one case.

Of the 11 patients, nine made a reasonably good recovery following operation; one patient's recovery is characterized as moderate owing to residual motor and sensory deficits, albeit insufficient to prevent light work; and one patient has made almost no recovery. One patient has been followed for 11 years, two for eight years, one for six years, one for three years, and two for one and a half years. The other four were lost track of shortly after operation, but appeared to be doing well at the time of discharge from the hospital. Of these seven patients who have been followed since operation, with one exception all have returned to gainful employment, or, if housewives, have returned to their work about home. In the case of the one patient who is known to have fared poorly since operation, approximately ten weeks elapsed between onset of symptoms of compression of cauda equina and operation. One and one-half years after operation this patient was still bed-ridden and showed almost no signs of recovery. Such a sharp discrepancy between the recovery experience of this patient and that of the other patients directs attention to the time interval between onset of the third stage and operation. Of the eight patients who came to operation within two weeks of sudden onset of compression of the cauda equina, all have made reasonably good recoveries. Less satisfactory was the recovery of a patient operated on approximately four weeks after onset of compression of the cauda equina; and almost no recovery has occurred in one case in which operation was delayed ten weeks.

Table 1 contains the pertinent data of the 11 cases, together with certain features which have not been mentioned in the text, such as the age and sex of the patients, and the spinal fluid total protein content.

SUMMARY

From an analysis of 11 examples of massive herniation of the nucleus pulposus with compression of the cauda equina, it is believed that certain features of the history aid accurate preoperative diagnosis.

Three stages in the history may be delineated. The first is characterized by chronic backache, the second by radiation of pain into one lower extremity, differing nowise from the common symptom of unilateral disc extrusion with implication usually of a single nerve root, and the third by relatively rapid, and ofttimes sudden, onset of symptoms indicating involvement of the cauda equina. Either of the first two stages may be absent. Patients presenting such a history, and in whom there is no clinical or roentgenographic evidence of implication of the spinal column by tumor or tuberculosis, may be pre-

Table 1

Patient	1	2	3	4	5	6	7	8	9	10	11
Age	46	44	52	27	58	27	53	37	34	62	55
Sex	M	M	F	F	M	M	M	F	F	M	M
History of injury to back	—	—	—	—	+	—	+	—	—	+	0
Chronic pain in back	+	—	+	+	—	+	+	+	+	—	+
(Duration)	(10 yr.)		(2 mo.)	(27 mo.)		(29 mo.)	(15 yr.)	(4 yr.)	(2 mo.)		(15-20 yr.)
Pain down one lower limb	+	+	—	+	+	—	+	—	+	+	+
(Duration)	(8 mo.)	(3 yr.)		(9 mo.)	(3 da.)		(4 mo.)		(1 mo.)	(2 wks.)	(6 mo.)
Sudden onset of pain in both lower limbs	+	+	+	+	+	+	+	+	+	+	+
(Duration to operation)	(10 da.)	(7 da.)	(23 da.)	(7 da.)	(1 da.)	(27 da.)	(43 da.)	(14 da.)	(11 da.)	(70 da.)	(1 da.)
Acute urinary retention	+	+	—	+	—	+	—	—	—	+	—
Bilateral sensory loss	+	+	— (Unilateral)	+	— (Unilateral)	+	— (Unilateral)	+	+	+	+
Bilateral weakness of feet and/or gluteal muscles	+	+	+	+	+	+	— (Unilateral)	— (Unilateral)	—	+	+
Loss of both ankle jerks	+	+	+	+	+	+	— (One obtained)	— (Both obtained)	+	+	+
Complete subarachnoid obstruction to radiopaque medium	Examination technically unsatisfactory	+	+	+	+	Not done	+	+	— (Incomplete)	+	+
Level of lumbar disc herniation	4	4	4	4	3	5	4	5	5	4	4
Total protein of spinal fluid (Mg. per 100 cc.)	186	65	120	60	56	319	84	96	69	Not done	Not done
Recovery	Good	Good	Good	Good	Good	Moderate	Good	Unknown (Good at time of discharge)	Good	Poor (Almost none)	Good

sumed to have a massive posterior herniation of an intervertebral disc.

Prompt surgical intervention is essential to satisfactory recovery. An instance is cited in which there was a prolonged period between onset of involvement of the cauda equina and operation. In this case almost no recovery has occurred, in contrast to reasonably good recoveries made by patients operated on soon after onset of compression of the cauda equina.

2100 Capitol Avenue.

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Cutaneous and Epidemic Diphtheria

ROBERT L. STERN, M.D., *Beverly Hills*

WITH diphtheria again a serious epidemic disease not only in California but reportedly worldwide, presentation of several important and not widely publicized facts regarding the disease and the cutaneous form is warranted. Experience with an epidemic of 133 cases, pharyngeal, cutaneous and combined in the Pacific in 1944[1] led the author to the following conclusions:

1. Diphtheria occurs widely in adults, even in those who previously gave no reaction to the Schick test. The patients in 33 cases had shown negative reactions to that test within two months previous to the onset of the disease. It must be remembered that immunity is relative only.

2. Cutaneous diphtheria is more common and much more important than has been realized. Indolent ulcers which give few symptoms may well act as a quiet source of virulent pharyngeal diphtheria. That skin lesions may be the original source for otherwise unexplained major epidemics is strongly evidenced by the following: Cutaneous diphtheria was eventually recognized as widespread in the indolent "desert or veldt sores" of armies in the African desert during the last war. In 1941 and 1942 many German soldiers were presumably sent from the desert to "rest" areas in Nazi occupied Northern countries, Norway, the Netherlands and back into Germany itself. The spectacular manifold rise in the diphtheria rates in these countries from 1940 to 1942 is shown graphically in the accompanying chart. At the same time the rates in the non-Nazi occupied adjacent

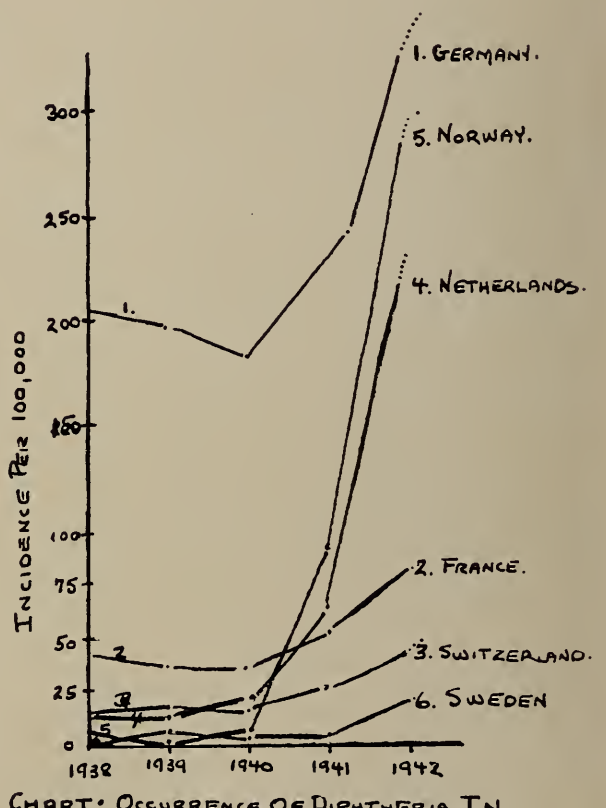


CHART: OCCURRENCE OF DIPHTHERIA IN EUROPEAN COUNTRIES: REPORTED CASES. DATA FROM BULLETIN U.S. ARMY MED. DEPT.; VOL I. NO 76. PP 104-108; MAY 1944.

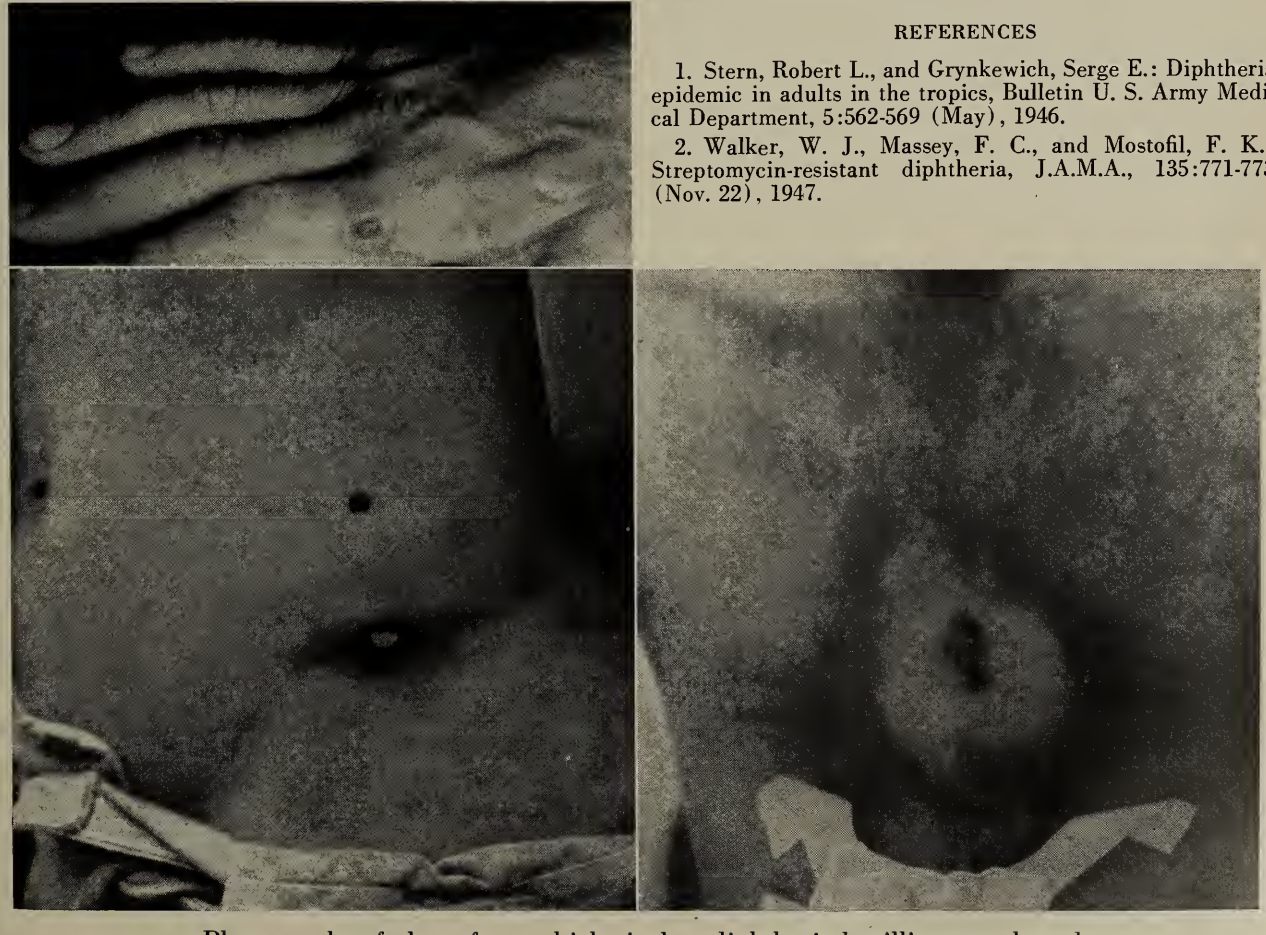
countries of Switzerland, Sweden and partially occupied France remained about the same or rose only a little. Also during the same period and later it was reported that sharply localized epidemics of diphtheria occurred amongst German prisoners of war brought to prison camps in the United States. Cutaneous and wound diphtheria has long been recognized, but the typical ulcers observed by the author (see photographs), almost all had the following fairly uniform characteristics: They were generally round or oval, varied from a few millimeters to 4 centimeters in diameter, had sharply demarcated "punched out" appearance with margins sharp or "rolled"; the base was flat and usually fairly clean but at times covered with a thin, greyish fibro-purulent layer or a thin, dry crust. The skin at the site of the ulcer was totally destroyed but the surrounding skin showed little reaction other than slight reddish to purplish discoloration.

The lesions were painless except when situated in areas involved in motion. They were usually on the extremities at the site of previous trauma such as abrasions, insect bites, scratches. A history of a small linear traumatic lesion gradually becoming a round or oval one was usual and most suspicious.

A most important point in diagnosis was that often when initial cultures from the lesions were negative for the diphtheria bacillus, after sterile wet saline compresses had been applied for from eight to 24 hours positive cultures were obtained. Any suspicious "negative" skin ulcer or lesion should have a wet dressing applied and the culture then repeated (or a compress applied before the initial culture). These ulcers when healed gave another characteristic finding, in that the scars were usually hypesthetic or anesthetic to pin-prick. This finding may be important in tracing cases of diphtheria.

3. Penicillin is of no proven use in diphtheria except in attempting to hasten the clearing of the pharyngeal carrier state and to hasten the healing of cutaneous ulcers. In our small experience with persistent pharyngeal carriers the value of adequate parenteral penicillin was questionable and gargles and sprays of solutions of 500 units per cc. also gave inconclusive results. Other more recent reports indicate a shortening for the carrier period by such topical use. In a recent report[2] of a case of fatal diphtheria treated with penicillin, streptomycin, and diphtheria antitoxin, it was stated that "there was no clinical or bacteriologic response to the administration of either penicillin or streptomycin." In our cases of cutaneous diphtheria, a penicillin solution of 500 units per cc. used on moist compresses was of definite value in shortening healing time of the lesions. Similar lesions did heal successfully, but more slowly, with the use of simple twice-daily sterile saline solution dressings and rest.

444 North Bedford Drive.



Photographs of ulcers from which virulent diphtheria bacilli were cultured

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The Berman Foreign-Body Locator

J. P. McBride, M.D., *Los Angeles*

THE Berman Foreign-Body Locator, developed by Samuel Berman, an electrical engineer, and J. J. Moorhead, both of New York City, is proving valuable as a supplement to the present indispensable methods of x-ray and fluoroscopy location of metallic foreign bodies embedded in tissues. Although it is well known that in many cases, foreign bodies, if they cause no symptoms, do not necessitate operation, removal of those that interfere with normal function usually is required. The surgeon, however, has undertaken the removal of such bodies from the deeper structures with reluctance, because of the difficulties involved in their detection and actual location on the operating table. Experience is proving the Berman locator to be especially helpful with all magnetic foreign bodies, except those which are extremely small. Its usefulness is also limited with large non-magnetic objects.*

The Berman locator, first used successfully in 1941, utilizes electronic principles to determine the location of metallic foreign bodies embedded in tissues. It is equipped with a meter on the control panel to indicate when a metallic body is near, and also with a horn that sounds with increasing intensity as the object is approached. The handling of the machine is simple, and it can be tuned properly and set in operation in only a few minutes.

A review of the literature is convincing that the Berman locator is a valuable adjunct to present methods. Parks[4] reports a case of a foreign body just proximal to the metacarpal phalangeal joint of the thumb. Although the locator led him to a point just over the extensor tendon, Dr. Parks, who had not previously used the machine, hesitated to incise the tendon sheath, for he could see no evidence of the foreign body. He called Mr. Berman for advice, and at his suggestion incised the tendon as the probe indicated. A small metallic body was easily removed.

Moorhead[3] records the removal of a small foreign body from the deltoid region after two previous attempts, without the help of the Berman locator, had failed. In another case a needle was removed from the left ventricle with the aid of the locator.

Skiles[6] reports two cases: In one a broken spinal syringe needle in the back was removed in 15 minutes with a minimum of trauma. In the second case a needle was embedded posterior to the patellar tendon. It was removed with little difficulty through the use of the locator.

Rieger[5] recounts a case in which a broken hypodermic needle deep in the pterygoid muscles was removed with the help of the Berman after a previous attempt without the locator had failed.

Minsky[2] and Alvis[1] report several cases in which intraocular foreign bodies were located with the assistance of the Berman locator, and removed.

In addition, this instrument has been found useful in connection with foreign bodies in the thorax, the abdomen, the neck, the brain, and the perineum.

The author's own experience with the Berman locator is confined to use in searching for foreign bodies in and about the structures of the eye. Although x-ray location of intraocular foreign bodies by the Sweet and Comberg methods has proved very satisfactory, it is not uncommon for x-ray to be in error a few millimeters in the exact location of such bodies. The following case report illustrates the usefulness of the Berman locator:

CASE REPORT

CASE 1.—The patient, while pounding a king-pin with a hammer, received a penetrating wound in the right eye. Examination showed a tiny corneal wound, 5 o'clock midway, an iris window, and an opaque lens. A roentgenogram, which located a metallic body 1x2x2.5 mm., 18 mm. back of the center of the cornea, 2 mm. below the horizontal plane, and 2 mm. to the temporal side of the vertical, placed the object in the posterior vitreous. At operation the lower temporal quadrant of the sclera was exposed. The Berman locator probe was applied to the sclera with no response. Then the magnet was applied to the exposed sclera for about one minute. Again the probe of the Berman instrument was employed, and a signal was obtained, indicating that the fragment was immediately under the sclera about 9 mm. from the limbus. An incision was made in the sclera with the graefe knife and the foreign body removed with the first application of the magnet to the incision.

Although it is likely that this foreign body could have been removed without the aid of the Berman locator, perhaps less trauma resulted than would have been caused by the usual method of making a scleral incision as near the foreign body as possible and depending on the magnet to pull it to the incision. When a foreign element is far back in the vitreous, one is at a loss to determine the exact site for making the scleral incision. In the case reported, it was gratifying that the splinter was immediately under the sclera as the instrument indicated.

CASE REPORT

CASE 2.—The patient had received a small penetrating wound over the ciliary body 4 mm. from the limbus, temporal side, right eye. The media of the eye were clear and no evidence of a foreign body was visible. When the Berman probe was applied to the globe in the wound area, the height of the response was noted directly over the wound. This indicated that a foreign body, probably magnetic, was in the eye in the region of the wound. The magnet was applied over the area, its pull being directed away from the lens, and a foreign body measuring 3x2x1 mm. was removed.

Again this fragment could have been removed without the Berman locator. However, knowledge

*The biplane fluoroscope developed by Leishman may also prove to be an additional aid in exact location at the time of operation.

given by the instrument that the foreign body was in the region of the wound was valuable; for a foreign body near the ciliary can damage the lens if pulled into it by the magnet, and save for the information given by the instrument, the operator would have hesitated to apply the magnet blindly without x-ray location.

CASE REPORT

CASE 3.—The patient had received a penetrating wound of the right eyelid. X-ray located a foreign body measuring 3x3x5 mm. in the upper nasal aspect of the right orbit posterior to the trochlea. The globe was not injured, and the wound healed with first intention. For 30 days the patient complained of pain about the eye and insisted on having the splinter removed. With the magnet applied as indicated by the Berman locator, the small metallic body was dislodged without much difficulty.

Here again the operator would have been reluctant to attempt removal without the Berman locator.

Regarding the detection of foreign bodies of various sizes and compositions, the following paragraph from a bulletin by Berman says:

"The distance from which a magnetic foreign body will be detected depends upon its size and composition. Soft iron and ordinary 'carbon' steel are the most responsive. Alloy steels such as ball-bearing steel and 'high speed' tool steel are less responsive. Certain stainless steel alloys are entirely non-magnetic and will give no response.

"The following distances apply to common iron or carbon steel:

Dia. of Mass	Approximate distance of detection from bare element (shield removed)
¼ mm.	2½ mm.
1 mm.	10 mm.
3 mm.	30 mm.
Common steel needle	1½ to 2 inches
3-inch iron nail	4 inches

"The sensitivity of the locator to non-magnetic metals (copper, brass, aluminum, lead, and so on) is relatively low and not always helpful. However, when a foreign body has been approached closely enough to be within detecting range of the probe and yet cannot be found, the locator can be most helpful.

"The following distances apply to non-magnetic metals:

0.45 caliber lead bullet	¾ inch
0.22 caliber lead bullet	⅛ inch
copper one-cent piece	1 inch"

The limitations of the Berman locator with extremely small magnetic intraocular foreign bodies is illustrated in the next two cases.

CASE REPORT

CASE 4.—The patient had received a tiny corneal wound in his right eye, 9 o'clock at the limbus. There was a window in the iris behind, a clear lens, and a visible shiny metallic foreign body lying on the retina in the dependent portion of the globe. There was no hemorrhage in the vitreous. An x-ray was reported as showing the foreign body, 0.5x0.5x1 mm., in the area where it was visible. The sclera was exposed in the midline below, and the inferior rectus was severed from the globe. The Berman probe gave no response, even after repeated applications. The magnet caused no sensation of pain. Yet the foreign body was clearly visible with the ophthalmoscope. Under direct vision the magnet was applied and the body noted to be magnetic, as it moved slightly with each application, though never out of its bed. A scleral incision was made within 2 mm. of the foreign body, but it could not be removed as it was apparently anchored securely to the sclera. For the next 30 days the eye was exposed daily to the giant magnet in an effort to increase the magnetism of the foreign body. After this period, another unsuccessful attempt was made to remove the fragment from the globe. The eye was lost. The Berman instrument proved to be of no value in this case, as a response was never elicited, even though the tip of the probe was within 1 mm. of a visibly magnetic foreign body.

By experimenting with foreign bodies of ½ mm. dimensions, the author has found that it is often necessary almost to touch the foreign body to obtain a response, which varies with the kind and size of the metal and its magnetism.

CASE REPORT

CASE 5.—The patient reported on the day of injury with a needle-like steel foreign body, measuring 0.5x0.5x4 mm., in the center of the vitreous, right eye. The media were clear and the fragment could be seen easily with the ophthalmoscope. The sclera was exposed and the Berman probe applied over a large area with no response. Under direct vision, the magnet was used and the foreign body was pulled to the lower temporal quadrant of the globe. Again the Berman probe was applied and a good response elicited. A scleral incision was made at the site of the greatest response, the magnet employed, and the foreign body easily removed. Upon healing, the eye was normal.

Experience in this case showed that it was necessary to bring the locator probe within 5 mm. of the object before gaining a response. This explains the lack of response when the foreign body was in the vitreous center.

CONCLUSIONS

The surgeon confronted with the removal of a metallic foreign body will do well to acquaint himself with the Berman Foreign-Body Locator, for it is a valuable adjunct to the present methods of location and removal.

1052 West 6th Street.

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CASE REPORTS

Drainage With an In-Dwelling Catheter Without Infection Following a Bladder Injury
Purpura Following Treatment With Tetraethylammonium Chloride
Streptomycin in Cryptococcosis
Carcinosarcoma

Drainage With an In-Dwelling Catheter Without Infection Following a Bladder Injury

THOMAS C. MCVEAGH, M.D., *South San Francisco*

IT APPEARS to be generally agreed that in cases requiring somewhat prolonged bladder drainage (e.g. acute neurogenic bladder, or bladder rupture or perforation) suprapubic drainage is preferable to use of the retained urethral catheter, because of the almost routine infection accompanying the latter.[1, 2, 3] The following case is reported because, among other things, it poses the question whether with the availability of penicillin and sulfonamides, this position may not be subject to revision.

CASE REPORT

A laborer, 29 years of age, examined about ten minutes after injury, said that he had fallen in a sitting position upon an upright steel reinforcing rod about 18 inches long and three-quarters inch in diameter. The rod had passed upward its entire length through the perineum, and the patient had pulled himself off the rod unassisted. A small amount of bloody urine was obtained by catheter. A roentgenogram taken with the patient in the semi-upright position showed no sub-diaphragmatic air. The patient was treated for shock and was operated upon almost immediately.

The abdomen was opened by a lower mid-line incision, and a perforation of the peritoneum overlying the right dome of the bladder was seen. When this area was isolated and stripped back a hole in the bladder was exposed. This was repaired by sutures of 0 chromic catgut. The overlying peritoneum was then repaired with a continuous suture of 000 chromic catgut.

Following this, the entire gastrointestinal tract was exposed and examined. No lesion of the colon or the small bowel could be found with the exception of a hematoma about one-half inch in diameter on the left lateral aspect of the ileum, near the mesenteric attachment and about 30 inches from the ileocecal junction. The bowel was plicated at this area to cover the hematoma. In the cul-de-sac there was found a piece of overall cloth about one-half inch in diameter, and a smaller piece of hair-covered skin which was apparently from the perineum. The cul-de-sac was cleaned out and the peritoneum was closed tight.

Following closure of the peritoneum, the space of Retzius was explored and through separate stab wounds on either side of the main incision soft rubber drains were inserted extraperitoneally to a point at the base of the bladder and prostate where it was assumed that the other wound of the bladder existed.

After closure of the abdominal wound the perineal area was cleaned and digital examination was performed. No lesion of the rectum could be found and the sphincter ani was uninjured. The wound tract was explored but could not be followed for more than one-half inch through the muscle apparently because of displacement of the wound tract by muscular movement subsequent to the injury. It appeared, therefore, that the rod had penetrated the perineum to the left of the anus, had passed upward along the side of the rectum, through the base of the bladder and out through the dome of the bladder on the right side into the peritoneal cavity, where the end of the rod had bruised the ileum, producing the bowel hematoma. The perineal wound tract was left open.

Postoperatively, the patient was given penicillin and a sulfa drug. The Foley catheter which had been inserted was retained and was connected to a low vacuum electric pump. Every effort was made to keep the bladder as nearly empty as possible at all times.

The postoperative course was smooth. The retention catheter was removed 14 days postoperatively, following which the patient voided without trouble.

Examination at discharge showed the abdominal wound and a small scar to the left of the anus both well healed. There was no urethral discharge and smears showed only epithelial cells. Urine was voided into three glasses and all specimens were clear. Chemical tests and microscopic examinations showed no abnormalities. There were no strictures and no residual urine.

The comment of the consulting urologist postoperatively was: "This patient has had a most unusual accident and a marvelous result. An in-dwelling catheter practically always is followed by infection. This man has what can be called 'virgin' urine. He has no strictures from infection in the posterior urethra. There is no infection in his bladder. The good results are due not only to the good surgery, but this happened to be a case where the newer biologics have proved to be true 'wonder drugs.'"

DISCUSSION

Following repair of the peritoneal perforation and closure of the abdomen, it was necessary to decide whether the bladder should be opened extraperitoneally. The catheter which had been introduced on admission was functioning well, the bleeding per catheter was not profuse and the wound in the base of the bladder was judged to be of such a nature (perforation) that it would close spontaneously if the bladder were kept decompressed. These considerations led to the choice of the retention catheter for decompression.

From the Department of Surgery, South San Francisco Hospital.

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Purpura Following Treatment With Tetraethylammonium Chloride

Franklin F. Ham, M.D., *Van Nuys*

THE purpose of this article is to report a case of thrombocytopenic purpura resulting from the parenteral administration of tetraethylammonium chloride *(Etamon*, Parke, Davis and Co.).

Although the toxic effects of tetraethylammonium chloride or bromide on laboratory animals have been studied extensively,[1, 2, 3] no allergic manifestations or ill effects upon the blood have been reported. Since the first use of the drug in man by Lyons and his associates[5] there have been several studies in human beings,[4, 6] none of which mention thrombocytopenic purpura as a possible complication of this treatment.

CASE REPORT

A white woman, aged 26 years, suffered a simple fracture of the right tibia with separation of the internal malleolus, on Feb. 9, 1946. The fractured limb was immobilized in a plaster cast for six months. After removal of the cast, the extremity appeared to be improving until about six months later (one year following the original injury), when it gradually became swollen, painful, cold, and extremely sensitive to touch. These symptoms persisted and grew progressively worse under conservative management elsewhere.

At the time of initial examination by the author, the right ankle was found to be swollen, mottled purple in color, exquisitely painful, moist to touch, cold, and with areas of hypesthesia and hyperesthesia not characteristic of peripheral nerve distribution. Roentgenographic examination showed a complete separation of the internal malleolus as a pseudarthrosis following the old fracture.

Operation was performed July 14, 1947, when the fractured malleolus was fixed in satisfactory position by means of a metallic screw. The cast was removed Aug. 11, 1947, and the patient instructed to bear weight on the foot on Sept. 2.

On Oct. 6, three months following operation, the patient complained of an exacerbation of the symptoms mentioned previously. The area was examined and the former findings confirmed. A diagnosis of reflex sympathetic dystrophy was made and a treatment program consisting of alternate hot and cold leg baths, massage, and Buerger's exercises twice daily was begun. One week later there had been no improvement and it was decided to use Etamon. Accordingly on Oct. 13, 14, 17 and 20 the patient was given a dose of 20 mg. per kg. of body weight (in each buttock 7 cc. of an aqueous solution containing 0.1 gm. of Etamon Chloride in each cc.). After these injections the swelling was dramatically relieved, the ankle was warm, bounding pulses were palpable, and the discoloration had disappeared.

On Nov. 23 the patient complained that the previous symptoms were recurring, although they were considerably milder than formerly. Another intramuscular injection of Etamon was given in the same dosage used in October. On Nov. 26 a purpuric eruption of the back developed without accompanying symptoms or evidence of bleeding elsewhere. A platelet count showed 99,220 per cubic mm. of blood. A second count on Nov. 26 showed 86,000 and a third on Nov 27 showed 91,005. The rash lasted about 72 hours and disappeared spontaneously. A platelet count on Dec. 11 was 161,000 and on Dec. 22 was 250,000.

A review of the history disclosed no other possible causative agent—the patient had taken no medicines of any kind for seven weeks preceding the first series of injections and for 11 weeks preceding the final one. There was no history of abnormal bleeding in the past and no history of personal or familial allergy. With the exception of the platelets, the constituents of the blood were normal on repeated examinations. There was no splenomegaly. Capillary fragility was not increased. Unfortunately, platelet counts were not made before the onset of purpura, but routine blood smears on July 14 and Oct. 10, 1947, were reported to show, respectively, that "platelets appear normal," and "platelets appear normal both numerically and morphologically."

It seems probable that this episode represents an allergic reaction to tetraethylammonium chloride characterized by a purpuric rash and an accompanying thrombocytopenia with spontaneous recovery.

6511 Van Nuys Boulevard.

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Streptomycin in Cryptococcosis

Houghton Gifford, M.D., and R. L. Hullinghorst, Lt. Col., M.C., *San Francisco*

THERE is still no known treatment of value in cases of torula meningitis. Shapiro and Neal[7] tried many therapeutic agents before the advent of sulfonamides and the antibiotics. They found none which in therapeutic doses would inhibit the growth of torula organisms. Others since then have been equally unsuccessful. Sulfonamides as well as penicillin have been tried in a few cases.[2, 4, 5, 8] However, in only one case[4] has there seemed to be indication that sulfonamides were of help, and no observers seem to have indicated penicillin as being of any aid.

Tests in vitro with sulfonamides and penicillin have shown no inhibition of growth activity of the organism, and these agents have not prolonged the life of mice injected with torula.[3, 8] Dawson and his co-workers list cryptococcus hominis as sensitive to penicillin. Robinson[6] found the organism insensitive in vitro to concentrations of 4,000 units of streptomycin and 250 units of streptothricin per cubic centimeter. In our own experience streptomycin in concentration of 25,000 micrograms per cc. has no inhibitory effect on in vitro growth of two strains of this organism tested.

Several factors make the trial of therapeutic agents difficult. There are at least 40 strains of torula organisms, eight of which are pathogenic. In addition, torulosis is infrequent. Voyles and Beck[8] in 1946 found 108 cases reported in the literature. In 54 of these only the central nervous system was involved. One rarely has a chance to treat a case of torulosis. Hence, only after a series of individual case reports can the value of a therapeutic agent be determined. The following, to the best of our knowledge, is the first case in which streptomycin has been used. This agent, and others, produced no noticeable effect on the outcome of the disease.

From the Laboratory Service, Letterman General Hospital, San Francisco, California.

CASE REPORT

The patient, a 22-year-old Hawaiian male, was in excellent health prior to Sept. 3, 1945. On that date he awoke with a stiff, painful neck, and painful involuntary muscular spasms of his arms. Blurring of vision was next noticed, accompanied by a pounding headache in the occipital region which radiated to the eyes. He had "spells in which everything went black and spun around" when he tried to walk. Two days later the left eye turned inward and double vision appeared. The patient was admitted to an army hospital Sept. 7, 1945.

Initial physical examination disclosed choked discs in the spine and left sixth cranial nerve paralysis. Subsequently two diopters papilledema developed and there was an apparent smoothing of the right side of his face. The tongue deviated slightly to the right and vermicular movements were present, most marked on the left. The jaw deviated to the right on chewing. When the patient was placed in the Romberg position, there was some swaying to the right and backward. Hyperesthesia was present in the posterior occipital region on the left, and there was tenderness to pressure over the vertebral spines, most pronounced at C7 and extending up to C2. No tendon reflexes could be obtained, even with reinforcement. However, the abdominal and cremasteric reflexes were present. The neck could not be flexed. Straight leg raising elicited pain at about 80°, most pronounced on the left. Erosion of the posterior clinoids was found. Electro-encephalography on Sept. 27 showed an abnormal focus, bi-occipital, more marked on the right. Results of serologic tests and urinalysis were normal.

Clinical impression was a posterior fossa tumor. Following confirmation by ventriculograms, craniotomy was done on Oct. 3, 1945, with exploration of the region of the cerebellum. The cerebellar tonsils were protruding into the foramen magnum, but no pathological process was evident to superficial inspection. The hemispheres were gently separated, and the exposed surface of the vermis had a yellowish-grey discoloration. A biopsy specimen was taken from this region, and the wound closed.

Pathological report revealed cerebellar hemorrhage, and questionable subdural hematoma. Examination of spinal fluid, not performed prior to operation due to clinical diagnosis, subsequently showed only the usual postoperative changes. Thereafter, the only abnormality was a gradual permanent increase in spinal fluid protein to a maximum of 352 mg. per cent on Dec. 10, 1945.

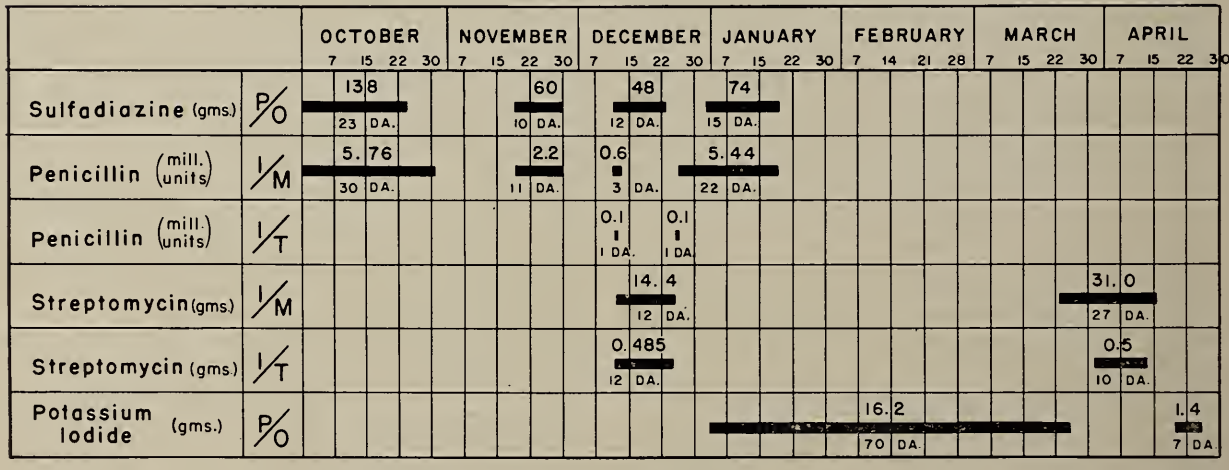
The biopsy specimen was judged to be inadequate, and exploration was again performed on Nov. 19, 1945. The cerebellar tonsils were separated, and extending into the fourth ventricle was an apparently neoplastic growth. Although this was poorly demarcated from normal tissue, as much of it as could be identified was removed and the wound again closed.

Pathological report revealed chronic granulomatous meningitis in which organisms typical of Cryptococcus hominis neoformans were seen. Six attempts at isolation of the torula organism from the spinal fluid by smear and culture were unsuccessful during the period from Dec. 14 to Jan. 22.

By Dec. 2, there was considerable bulging at the operative site, and the wound was thinned out on the left side and threatening to rupture. Lumbar punctures were done daily to relieve the pressure, but on Jan. 3, 1946, the wound broke down and a cerebrospinal fluid fistula developed. On Jan. 4 the fistula was excised and the wound was closed. A ureteral catheter was left in the subdural space to drain the excess fluid, and the wound healed without further difficulty.

The patient showed considerable improvement, was up and active until the last of March, 1946, when signs of increased intracranial pressure developed. These were relieved with daily drainage of cerebrospinal fluids, but more and more frequent drainage became necessary and the response was less beneficial. On April 26, 1946, the patient died of medullary decompensation secondary to the increased intracranial pressure.

SUMMARY OF TREATMENT



TOTAL DOSAGE:

Sulfadiazine	(Per Os)	320	gms.
Penicillin	(Intramuscular)	14.0	million units
Penicillin	(Intrathecal)	0.2	million units
Streptomycin	(Intramuscular)	45.4	gms.
Streptomycin	(Intrathecal)	0.985	gms.
Potassium Iodide	(Per Os)	17.6	gms.

With the exception of the immediate postoperative periods, the patient had fever ranging from 99° F. to 101° F. The therapeutic agents used in treatment are noted in the accompanying chart.

Penicillin and sulfadiazine were administered at the beginning for a 30-day period in the customary prophylaxis associated with craniotomy. The same regime was used for a ten-day period associated with the second operation.

In December, a small amount of streptomycin having become available, 0.485 gm. was administered intrathecally in doses ranging from 0.06 to 0.125 gm. over a 12-day period. Every three hours 0.125 gm. was given intramuscularly for a total of 14.4 gm. When the supply of streptomycin was exhausted, combined sulfadiazine and penicillin therapy was resumed for the next 22 days.

In late March, the patient again appeared to be failing and streptomycin was given again intramuscularly, and continued for 27 days with a total dose of 31 gm. During the last two weeks the drug was injected subdurally, after aspiration decompression, in doses of 0.125 gm. to 0.25 gm. on three occasions.

The following levels of streptomycin were obtained in the blood and spinal fluid:

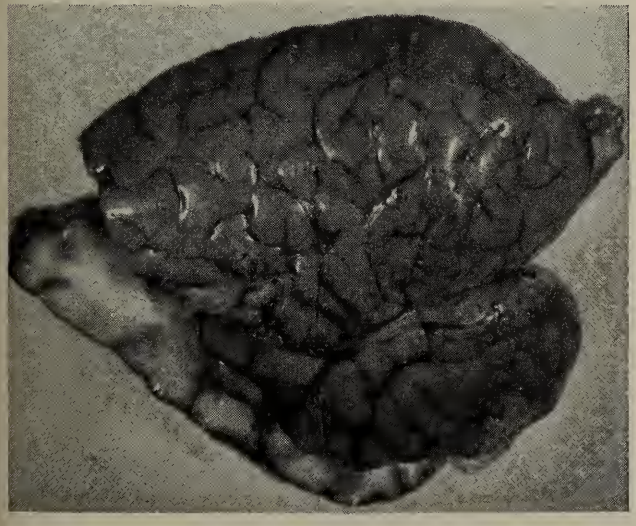
STREPTOMYCIN LEVELS

Units per cc.

Date	Blood	Spinal Fluid
9 April	16	2
11 April	64	96
12 April	..	126
15 April	..	6
16 April	40	4
17 April	..	4
20 April	.. less than	1

AUTOPSY FINDINGS

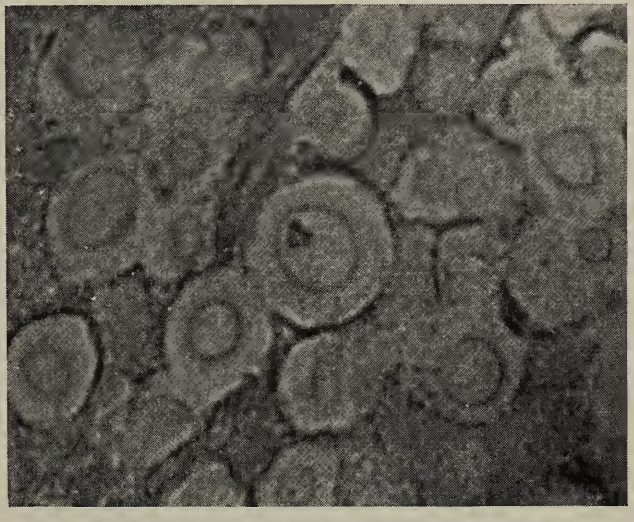
With the exception of an acute bronchiolitis and concomitant bronchopneumonia, the significant findings at autopsy were limited to the central nervous system. The dura mater was tense and firmly adherent, at the present operative sites, to the right cerebellar hemisphere. Over the base of the brain, particularly in the region of the optic chiasm and the brain stem, the leptomeninges were thickened and opaque. Numerous firm white nodules, 1 to 3 mm. in diameter, were present in the leptomeninges here, and were scattered over the rest of the brain and spinal cord. Microscopically these nodules were composed of single or multiple granulomata. Each granuloma had a firm, often hyalinized fibrous wall, on the inner surface of which were arranged epithelioid cells enclosing a small caseous center. A zone of lymphocytes and plasma cells surrounded the entire granuloma. Scattered multinucleated giant cells were present in the wall, and many typical budding yeast-like organisms with a thick gelatinous capsule were present within the wall and the central caseous area. These focal granulomata showed a predilection for the perivascular zones of the larger meningeal vessels.



Brain: Focal granulomata of leptomeninges.



Tubercle showing torula organisms in caseating center x135.



Torula organisms showing prominent mucoid capsule x600.

The remainder of the brain showed focal perivascular and perineuronal edema with moderate congestion. Occasional perivascular hemorrhages were noted. Scattered small cortical vessels showed perivascular cuffing by lymphocytes and polymorphonuclears.

CONCLUSIONS

1. A case of chronic proliferative meningitis due to Cryptococcus hominis neoformans is reported.

2. Clinical trials of sulfadiazine, penicillin, and streptomycin did not prevent death.

139 Hugo Street.

Photographs are from the Letterman General Hospital Photographic Laboratory.

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Carcinosarcoma

Orville F. Grimes, M.D., and H. Glenn Bell, M.D.,
San Francisco

PERHAPS no subject in medicine has incited such a wealth of controversy as have the so-called carcinosarcomas. Although their existence was not doubted by early investigators, present-day opinions concerning their nature vary considerably. Certainly there are some tumors whose histologic characteristics suggest that they arise from the atypical growth of more than one cell type. Virchow[13] described their dual nature; he believed that within the primary carcinoma or sarcoma the stroma or the epithelial elements respectively were simultaneously or subsequently stimulated to malignant growth.

Herxheimer[6] believed that carcinoma cells stimulated an excessive growth of the stroma and that when proliferation of the stroma reached a malignant stage the tumor became a carcinosarcoma. Meyer[8] presented a simple yet thorough approach to these tumors by classifying them into three groups: "collision tumors," two independent tumors which invade each other, "combination tumors," produced by the growth of two different blastomatous portions derived from one stem cell, and "composition tumors," those in which both parenchyma and stroma have become blastomatous.

Ewing[3] considered no single explanation applicable to all cases, observing that transformation of epithelial cells into spindle cells or the misinterpretation of spindle-shaped epithelial cells as connective tissue cells might well account for the histologic characteristics of these tumors. Karsner[7] mentioned that reactionary connective tissue growth may lead to the elongation of epithelial cells. The extreme morphological variability in some carcinomas makes one hesitate before ascribing a dual nature to such tumors.

Only five case reports appear in the literature in which the skin was the source of so-called carcinosarcoma. For mixed malignant tumors arising in other organs of the body a definite embryologic basis exists. The Wilm's tumor, for example, is a developmental one and is best called an embryonal mixed tumor. The association of epithelial and connective tissue elements is explained by the fact that the epithelium of the urinary tract is derived from mesoderm, while the convoluted tubules develop from undifferentiated mesenchyma having the appearance of connective tissue in which glandular elements are formed (Boyd[1]). In the uterus the relationship of mixed tumors to displaced mesodermal embryologic rests is well established. Mixed malignant tumors arising from the skin have no such developmental derivation. These are mixed tumors arising in adult life without a congenital basis. The distinction between the two types should be emphasized.

The authors have recently treated a patient with a carcinosarcoma which developed in an old burn cicatrix of the arm.

CASE REPORT

The patient, a 48-year-old unmarried farm laborer, entered the University of California Hospital March 19, 1947, stating that at the age of six he had been burned extensively over the left chest, arm, axilla and flank. The wound, treated without skin grafting, resulted in diffuse scarring of these areas. The scar was most dense on the outer surface of the upper arm. Small crust formation had begun in one area of the scar 18 months prior to entry to the hospital. This lesion healed and recurred several times until August, 1946, when a crust-like lesion appeared which did not heal with the passage of time. The patient had received local treatment elsewhere, and when a small polypoid growth appeared in September, 1946, it was excised at the base. The polyp shortly reappeared and in December, 1946, a second excision was performed with pinch grafting of the resected base. The area did not heal in spite of the skin grafts; instead the polyp continued to grow at a rapid rate.

Examination at the time the patient was first admitted to the University of California Hospital revealed a dense scar which occupied the left upper outer arm, axilla, posterolateral aspect of the chest and the left flank. A soft, red, friable, fungating mass the size of an orange (10 by 8 by 7 cm.) was present on the lateral aspect of the arm just above the elbow (Figure 1). It was attached to the skin by a narrow pedicle. Brisk hemorrhage occurred with the slightest amount of handling. Small firm lymph nodes were present in both axillae. A roentgenogram of the chest showed no parenchymal or bony abnormalities.

The patient refused to undergo a shoulder girdle amputation and a compromise was effected. On April 2, 1947, the tumor together with a large amount of surrounding scar was removed. The deep dissection was carried to the level of the fascia and a small bit of triceps muscle was removed in that area where the tumor seemed to be invading most deeply. The resulting wound was repaired by a graft of skin of intermediate thickness procured from the thigh.

Examination of the specimen showed no gross evidence of invasion into the muscular tissue, although the tissue was constricted somewhat in the area subjacent to the tumor. Microscopically the skin pedicle showed an abrupt change from the marginal stratified squamous epithelium into an area wherein the squamous cells became hyperchromatic, pleomorphic, and showed invasion into the dermis and subcutaneous tissue. The epithelial cells were arranged in irregular cords and ringlets extending for a short distance into a cellular mass of interlacing, whorl-like structures. The component cells of this latter tissue were spindle shaped for the most part and contained spindle shaped or oval nuclei most of which exhibited a vesicular arrangement of their chromatic networks. Many mitotic figures were seen. A diagnosis of squamous cell carcinoma and fibrosarcoma arising in an old skin (burn) scar was made (Figure 2).

From the Department of Surgery, University of California Medical School, San Francisco.

By May 5, 1947, one month after primary excision, the grafted area had completely healed. However, in the short period of one week a rounded, polypoid, red, friable, golf-ball sized mass reappeared at the site of the original tumor. A small portion of this mass was removed for histologic study. Microscopically a thin layer of stratified squamous epithelium overlay a large mass of cells exhibiting an irregular interlacing and whorl-like pattern with only a minimal amount of stroma. The individual cells exhibited a marked degree of pleomorphism and were distinctly hyperchromatic. The nuclei were ovoid or cigar-shaped, closely packed, and exhibited a vesicular arrangement of their chromatin networks. Many mitotic figures were present. A diagnosis of recurrent fibrosarcoma was made (Figure 3).

A roentgenogram of the chest again showed no evidence of pulmonary spread. The problem was discussed fully with the patient, who consented to an interscapulo-thoracic amputation of the left upper extremity, which was performed on May 27, 1947. Histologic examination of the tumor showed a picture identical with that seen in the biopsy specimen (Figure 3). The many axillary lymph nodes showed extensive lymphoid and reticular hyperplasia, but no involvement by metastatic tumor tissue.

DISCUSSION

Mixed malignant tumors have been extensively discussed in the literature. Since the time of Virchow their exact nature and indeed even their existence have been the subject of much controversy. Most modern investigators believe that rather than being tumors of dual origin, these lesions represent either carcinomas or sarcomas which assume characteristics of sarcoma or carcinoma respectively, mainly by exhibiting morphological variations in the primary type of cell. However, Harvey and Hamilton[5] reporting recently, express the belief that their dual nature is a specific entity and explain the sarcomatous elements by the fact that the cells of the stroma are stimulated to a malignant state by the carcinoma cells. This view is supported by the experimental work of Ehrlich and Apolant[2] who, while transplanting carcinomas into the breasts of mice, found that in the tenth generation a different histological picture appeared, showing malignancy of both epithelial and connective tissue



Figure 1.—The large cauliflower-like tumor occupied the inner surface of the upper arm in the region of the elbow. The extremely friable, deeply red tissue bled after the slightest trauma. Areas of superficial necrosis alternate with areas having the appearance of old granulation tissue.

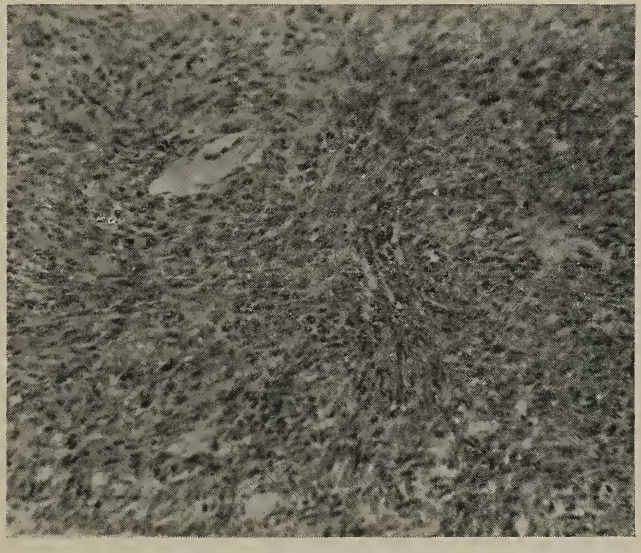


Figure 3.—Photomicrograph of tissue which reappeared one month after wide local excision of the original tumor. Note the definite sarcomatous nature and the apparent greater degree of malignancy. No malignant epithelial elements were present in this tissue.

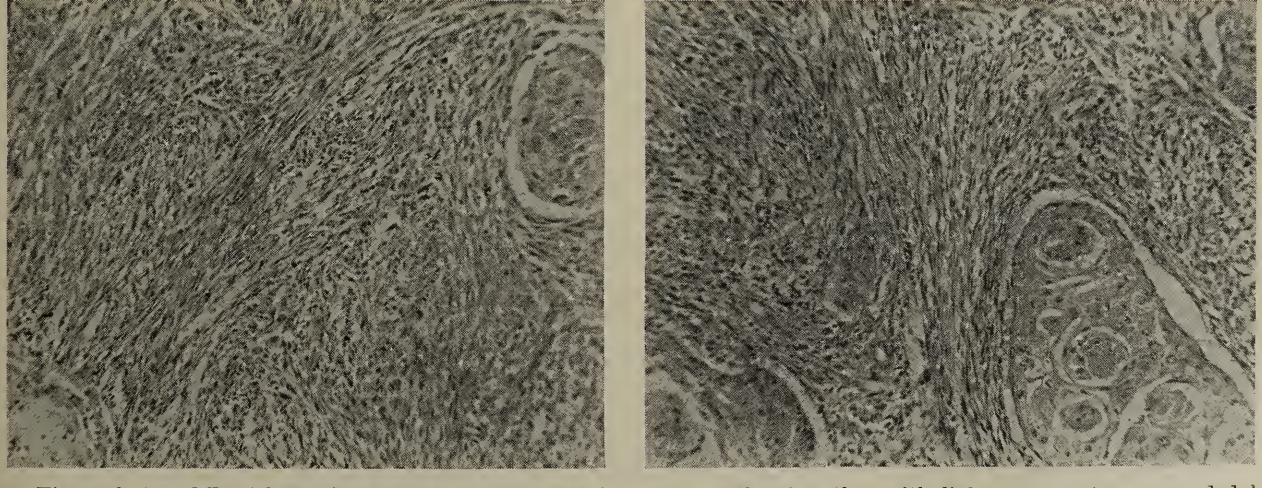


Figure 2, A and B.—Photomicrographs of two areas of the tumor showing the epithelial components surrounded by interlacing strands of spindle-shaped cells which form whorl-like structures in some areas. The contrast between epithelial and connective tissue elements is marked.

element. Russell[11] reported a similar phenomenon and mentioned that once the sarcomatous element began it tended to eliminate the carcinomatous element. Nicholson[9] reported the development of carcinoma while transplanting sarcoma in the rat.

At the opposite extreme are those who believe that true mixed malignancies as such never, or at least extremely rarely, exist. Ewing objected rather mildly to the use of the term to indicate them as distinct entities, stating that the transformation of epithelial cells into spindle-shaped cells occurs commonly in epithelial tumors. This change is facilitated by rapid growth of the tumor, relief from pressure, and by the presence of an inflammatory exudate. Karsner also mentions that reactionary connective tissue growth may lead to the elongation of the cells. Pearlman,[10] reviewing the 17 cases of carcinosarcoma of the esophagus reported as such in the world literature, concludes that these tumors are actually anaplastic carcinomas or squamous cell carcinomas with transitional cell features. The transitional cells are frequently elongated and spindle-shaped and can easily be confused with sarcoma cells. Saphir and Vass,[12] in an exhaustive review of the subject, conclude that the carcinosarcomas reported in the literature can be interpreted as sarcomas on the basis of morphologic cellular variation. Carcinoma, when accompanied by chronic inflammatory changes, produces a dense cellular stroma which perhaps compresses the epithelial cells. Inflammatory changes are most marked in those organs exhibiting cyclic changes, such as the uterus, breast, and thyroid. It seems more than casual circumstance that most carcinosarcomas occur in these organs. These tumors may also result from the invasion of a pre-existing benign connective tissue tumor by carcinoma. The young fibroblasts perhaps are interpreted as sarcoma cells. Frank and Lev[4] studied five cases of carcinosarcoma of the larynx at the Michael Reese Hospital and reviewed similar case reports from the literature. They conclude that all the tumors, including those that they themselves had previously reported as carcinosarcomas, were actually carcinomas which had undergone morphological variations. The morphological similarity of some transitional cell carcinomas of the bladder to spindle cell sarcoma is well known. Certainly, then, there is no unanimity of opinion concerning the existence of these tumors as specific entities.

Five case reports of carcinosarcoma arising from the skin have appeared in the world literature. One tumor developed in an area of dermatitis produced by irradiation; the second was a metastatic tumor from a previously unidentified tumor of the lip; the third arose in a joint fistula. The other two cases were basal cell carcinomas whose deeper portions consisted of spindle cells in an abundant connective tissue stroma exhibiting chronic inflammation. Saphir and Vass cast doubt concerning the authenticity of these tumors, indicating that their appearance can be explained either by the well-known morphological variations of epithelial cells or by the misinterpretation of chronically inflamed connective tissue cells as sarcoma cells. We believe that in the case we report herein, the histologic picture is so definite that the tumor must be of dual origin. The presence of definite carcinomatous and sarcomatous elements in the tumor excised locally, together with the fact that the recurrence showed a definite sarcomatous pattern, bears out this contention.

CONCLUSIONS

Most present-day investigators believe that carcinosarcomas are not distinct entities, although no unanimity of opinion prevails. The morphological variations of carcinoma cells, some of which assume spindle shape, may explain some of those cases wherein a sarcoma as well as a carcinoma is diagnosed. This is especially true of squamous cell carcinoma with transitional cell features. Chronic inflammation may produce morphologic changes in tumor cells which may be falsely interpreted as portions of a malignant connective tissue tumor. Also, a lymphocytic reaction is sometimes provoked which may be interpreted as a lymphosarcomatous element. Invasion of a benign connective tissue tumor by carcinoma or the invasion of a benign adenomatous tumor by sarcoma may explain some of the misinterpretations. In spite of these facts and opinions there exist those cases wherein any of or all these factors cannot adequately explain the precise histologic picture of both carcinoma and sarcoma occurring in the same tumor.

SUMMARY

A brief review of this definitely controversial subject only emphasizes the lack of unanimity of opinion concerning the nature and indeed the existence of those tumors known in the literature as carcinosarcomas. The case history of a patient presenting a tumor composed of both squamous cell and fibrosarcomatous components is reported. No attempt is made to verify or disprove previously reported opinions referable to the subject.

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MEDICAL PROGRESS:

Newer Methods of Treatment of Leukemias and Lymphomas

HOWARD R. BIERMAN, M.D., *San Francisco*

LYMPHOMAS and leukemias have emerged as a group of closely allied conditions, characterized by a progressive proliferation of the lymphoid and other hematopoietic tissue elements. These diseases may be depicted as dynamic conditions frequently exhibiting similar characteristics (Figure 1).

The cessation of World War II has seen a great impetus in the application of newer methods of treating lymphomas and leukemias. The most notable single advance has been in the field of chemotherapeutic agents, namely the amine mustards and urethane. Many other chemical agents are being used in the treatment of these neoplastic diseases. Their efficacy eventually will be determined by the test of time. However, the immediate evaluation of any anti-neoplastic agents must be judged carefully, employing the criteria of prolongation of life, change in tumor size, alteration of the signs and symptoms, and observation of the general course of the disease. These methods of treatment may be listed as curative, arresting or palliative, and will be so designated.

A *curative agent* or procedure is defined as one that completely removes all traces of the neoplastic process, resulting in permanent alleviation of such symptoms or signs attributable to a neoplasm.

An *arresting agent* significantly alters the natural course of the neoplastic disease favorably so that temporarily the symptoms or signs due to the neoplasm disappear, and the patient returns to a relatively normal state although some neoplastic tissue remains viable in situ.

A *palliative agent* or therapy is essentially one which alleviates the effects of the neoplastic disease upon the patient, although the symptoms, signs, and course of the disease remain unaltered and the progress of the disease continues unabated.

There have been recent advances in the field of therapy in this group of diseases which encompass surgical operations as well as irradiation. It is perhaps best to discuss each innovation in turn.

I. SURGICAL OPERATIONS

It has become increasingly apparent that some forms of lymphoma may have a unicentric origin. The recorded cases of long survival following surgical extirpation with or without massive irradiation are support for this concept.[9] One can state in the light of our present knowledge concerning the origin of the lymphomas that a single focus of involvement, without evidence or suspicion of involvement of any other area by available techniques, should be treated by wide surgical excision,[2] and should be followed by a maximum amount of x-ray until further evaluation proves the latter to be of no additional value.

From the Laboratory of Experimental Oncology, University of California Medical School, San Francisco, and the National Cancer Institute, National Institute of Health, United States Public Health Service.

II. RADIOTHERAPY

A. *Irradiation:*

In the localized involvement of areas by the lymphomas which are not amenable to complete surgical removal, intensive x-ray irradiation is recommended. The manner of administration depends upon the condition to be treated.

Therapy depends upon localization of the area of involvement of the lymphoma; thus irradiation to peripheral areas or the visceral regions is guided by the location of the masses. Total body irradiation is preferred by many radiologists in the therapy of chronic leukemias, often combined with localized irradiation to the enlarged spleen.[26] X-ray irradiation in any form has generally proven of little value, and possibly of injurious effect, in the acute leukemias. However, in some cases very small doses may prove palliative.

Special methods of irradiation to long bones and vertebrae result in notable changes in the peripheral blood as well as in marrow depression, but there is no specific effect upon the non-irradiated areas of involvement such as peripheral adenopathy, cutaneous infiltration or visceral masses.

B. *Radium Implantation:*

The requirement of highly trained personnel with wide experience, and the lack of advantage over the use of local irradiation have removed radium from the list of agents to be recommended in the treatment of lymphoma.

C. *Radioactive Substances:*

Various radioactive isotopes of phosphorus (P^{32}), strontium (Sr^{85}), silver (Ag^{111}), gold (Au^{198}), and others, have shown some affinity for various neoplastic tissues. However, the selective deposition of such substances is too small for radiotherapeutic effect without untoward damage to normal tissue. The over-all use of radioactive isotopes in therapy for lymphomas does not appear to hold any particular advantage over x-ray irradiation. They offer merely an additional route to administer radiation. However, there does appear to be some advantage to P^{32} in the treatment of chronic myelogenous leukemia.[13] The material may be given orally, and radiation sickness is stated to be much less than that caused by x-ray radiation. The lack of a true comparison of the action of comparable doses with both

methods, however, limits this observation. Again, because of the relative difficulty in obtaining and handling the radioactive material, and the need for special facilities and experience, use of it is limited to research institutions. The general availability of x-ray equipment forces the conclusion that x-ray irradiation is the treatment of choice in general medicine at this time.

Recently, radioactive colloidal gold (Au^{198}) has been used by local injection into masses of neoplastic diseases, and also by localization of the material in the reticulo-endothelial system.[7,21] The advantages of this procedure are doubtful, and much longer and better evaluation is needed. Indeed, there is evidence to support a critical attitude that such therapy is inferior to present methods.

III. CHEMOTHERAPY

A. *The Amine Mustards:* These compounds are closely related to mustard gas, and have been shown to have a primary nucleotoxic and cytotoxic action causing necrosis of lymphoid tissue with notable myeloid depression of the bone marrow.[6] During the past four years, these agents have had wide trial in many laboratories, our own included. The nitrogen mustards have been shown to be effective in reducing the peripheral as well as the visceral masses of Hodgkin's disease and giant follicular lymphoma. This effect is not permanent, and relapses often occur within one to six months following a single course of therapy. The most beneficial effect occurs in cases of Hodgkin's disease, although return of signs and symptoms occur within a period of six weeks in approximately 40 per cent of cases. The nitrogen mustards have produced spectacular though temporary improvement in patients with mycosis fungoides. Lymphosarcoma and the chronic leukemias when treated with the nitrogen mustard have shown initial transient improvement, but of shorter duration than that obtained in Hodgkin's disease and giant follicular lymphoma. The effect in acute leukemias has been disappointing.

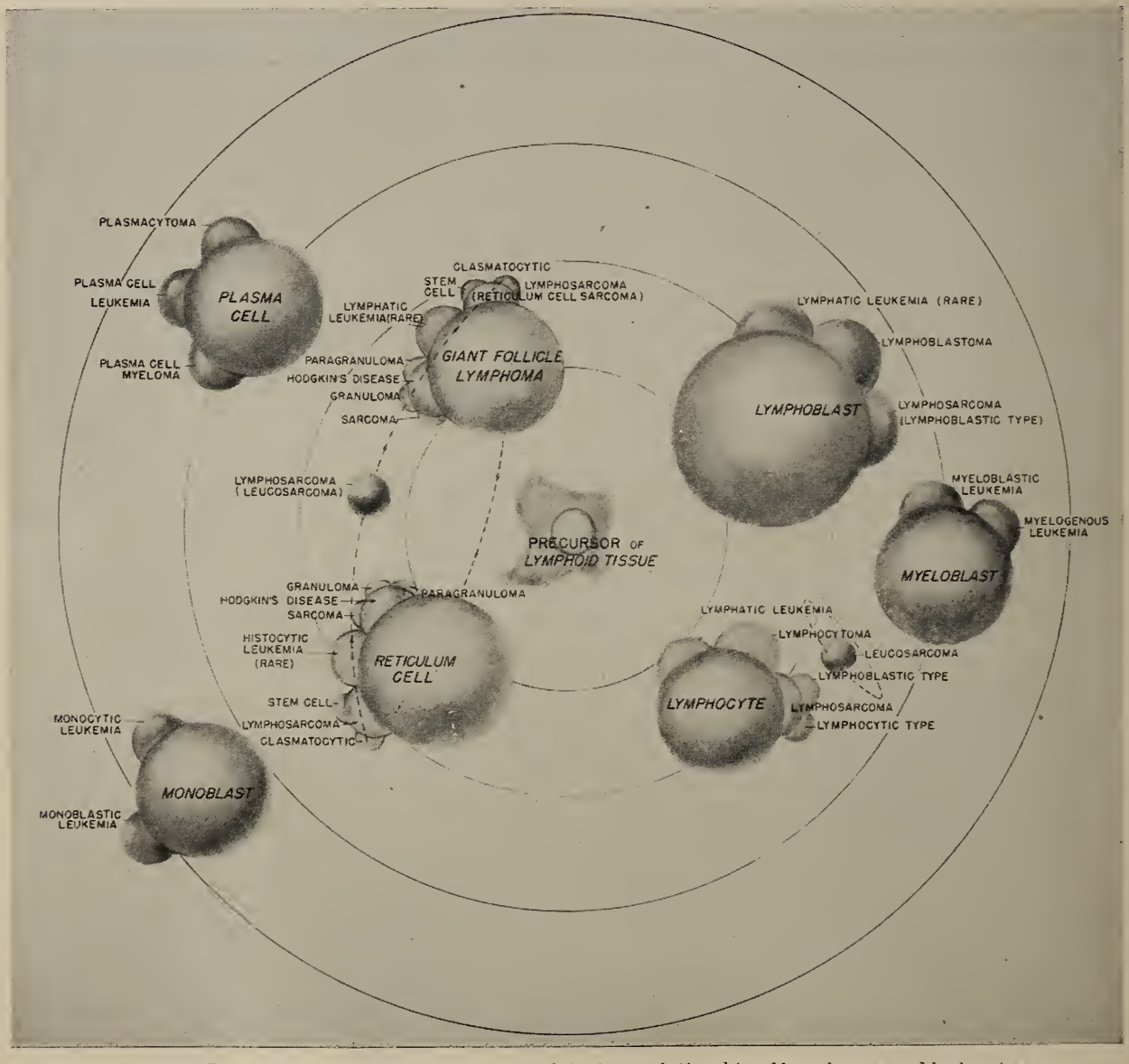


Figure 1.—Dynamic schematic representation of the interrelationship of lymphomas and leukemias.

One can summarize the results to date as follows:

Methyl bis (Betachloroethyl) amine (HN2) and tris (Betachloroethyl) amine (HN3) administered intravenously in appropriate doses have altered the natural course of Hodgkin's disease in many cases.

Approximately 90 per cent of patients with Hodgkin's disease previously untreated will respond favorably to HN2 by prompt regression of fever, adenopathy, splenomegaly and hepatomegaly accompanied by a disappearance of most of the symptoms of the disease (pruritus, anorexia, malaise, weakness), and a return to a sense of well-being for periods of one to six months.[1]

Approximately 70 per cent of patients with Hodgkin's disease previously treated with x-ray and responding favorably at the time of HN2 therapy, also respond favorably to the nitrogen mustard therapy.

In general, only 55 per cent of patients with Hodgkin's disease will respond favorably to HN2 if they were no longer responding to x-ray therapy, and the duration of remission is short.

Longer remissions can be produced by more aggressive dosage, but the hazard of severe, prolonged granulopenia and thrombopenia increases proportionately.

Although HN2 remains experimental, there is increasing evidence that it may be used as a temporary arresting agent in the generalized forms of lymphoma, especially Hodgkin's disease, mycosis fungoides, and giant follicular lymphoma.

Lymphosarcoma and the leukemias have shown a brief but transient response to HN2.

The granulopenic effects of HN2 can be effectively controlled by penicillin, but the coagulation defect remains a major problem despite whole blood transfusions, protamine, toluidine blue and other fluorescein dyes.[23] With the large number of analogs of HN2 that may be available soon, the future is encouraging.

B. *Urethane:* Urethane has been used in human studies for approximately four years, although its effect as a mitosis arrestor has been known for at least 20 years.[20] This agent inhibits mitosis of the immature cells. It is most effective in chronic myelogenous leukemia, producing a decrease of the total leukocyte count toward normal limits, although the responses to this agent are by no means constant. The hemogram returns toward the normal, generally accompanied by a decrease in the size of the spleen and peripheral lymphadenopathy. In some individuals who have an anemia, there may be a rise in the hemoglobin level. However, all the changes have proven reversible, and no permanent benefit has resulted in any case. There has been no favorable permanent effect of urethane on any of the lymphomas or other neoplastic diseases.

C. *Arsenic:* Fowler's Solution (Sodium Arsenite) remains a useful agent in the treatment of some leukemias, chiefly in chronic myelogenous leukemia. It is inexpensive and readily available, a consideration if x-ray irradiation is either difficult or impossible to obtain. Precaution must be exercised to prevent excessive toxic effects upon the bone marrow, and repeated blood studies at frequent intervals are necessary.

Radioactive arsenic (As) has been used in an effort to combine irradiation with the selective chemical effect of arsenic.[11] The relatively small amount of arsenic administered in such circumstances is below the effective chemical dose, and practical results have not supported the theoretical contention.

D. *Folic Acid Derivatives:* On the basis of the favorable mouse tumor studies,[3,14,15] Farber and his co-workers studied the effect of pteroyldiglutamic acid and pteroyltriglutamic acid in 90 patients with advanced neoplastic diseases.[4] Daily doses of from 20 to 500 mg. intravenously or 10 to 150 mg. intramuscularly were used. Pteroyldiglutamic acid was given intramuscularly in 50 to 250 mg. daily doses or 20 to 300 mg. orally each day.

No important untoward reactions were reported with either intramuscular or intravenous administration. A few patients experienced improvement in energy, appetite, sense of well-being, and less irritability and apprehension. In one case there was temporary decrease in the size of multiple subcutaneous nodules of a melanotic carcinoma; in another, temporary decrease in size of metastases to the lung from a carcinoma of the testis; and in two others in which there were bone metastases from prostatic carcinomas, blood acid phosphatase returned to normal, but these changes were not constant.

Temporary regressions in symptoms and in metastases, as well as fluctuations of the acid phosphatase level in the blood in patients with carcinoma of the prostate are not uncommon. However, under other means of treatment, these changes cannot be accepted as indisputable proof of any definitive effect of an agent, favorable or otherwise, upon cancer patients.

In our limited experience with these compounds, administered separately and in conjunction with other chemotherapeutic agents, they have shown no objective favorable effect. This is in agreement with other reports.

E. *Antifolic Acid Compounds:* The antifolic acid compounds have also shown some promise in animal experimental studies, but investigations in human beings are far too preliminary for comment.

Unlike the relatively non-toxic diglutamic and triglutamic acid derivatives, the 4-amino-pteroylglutamic acid compound has been shown to depress the hematopoietic system, and must be used by investigators with extreme caution.[12]

Temporary remissions occurred in 10 of 16 children with acute leukemia following the administration of this agent.[5] At the time of reporting, the hematologic and pathologic improvement had continued for only three months. The administration of 4-amino-pteroylglutamic acid (aminopterin) will produce a refractory pancytopenia and the authors stress the toxicity along with the fact that the remissions must not be regarded as cures. It is to be noted that spontaneous remissions both complete and

of considerable duration may occur in acute leukemia.[10] At present, this compound may be considered an arresting agent. Future development in this direction appears promising.

F. *Thiouracil:* Thiouracil has been shown to be of no definite value in the therapy of leukemias.[16]

G. *Sulfapyridine:* The rapid leukopenia which occurs within 12 to 18 hours after giving sulfapyridine in some leukemias has been shown to be transitory, and not attributable to a toxic granulopenia. This suggested a specific effect of sulfapyridine upon the leukemic lymphocyte, but as yet it remains of unproven efficacy in this condition.[17]

H. *Myelokentric and Lymphokentric Acids:* These extracts of the excreta of patients with the myelogenous and lymphogenous leukemias have shown some equivocal effects upon patients with leukemia,[19] and the value of them remains to be established. The extracts are difficult to obtain; evaluation of their effect is even more difficult, and much further investigation is needed.

I. *Colchicine:* This agent is known for its mitosis arresting quality, and although it has been used widely in animal experiments, there have been few adequate studies of effects on humans. The results obtained in a few human studies, however, have been disappointing in that toxicity of the compound far overshadows any favorable effect of the drug on the neoplastic processes.

J. *Trypanosome Cruzi Vaccine (KR):* The Klueva-Roskin Vaccine (KR) made from cultures of trypanosome cruzi has been investigated in no less than three laboratories. Despite a favorable report on this agent in mouse tumors, as yet there has been no confirmation of the reported Russian successes in human beings with this agent.[8,18]

K. *Desoxypyridoxine:* The use of antipyridoxine agents, such as desoxypyridoxine, along with vitamin B_6 deficiency to reduce the bulk of lymphoid tissue has proven effective in animals. Results of their use in patients again is preliminary, and indications to date are not encouraging.[25,27]

L. *Antireticular Cytotoxic Serum—ACS:* Some improvement in patients with Hodgkin's disease has been reported following the use of ACS.[22] A longer period of evaluation with more definite data is needed. The progress with this agent must be viewed with interest, but as yet its use remains experimental.

M. *Stilbamidine:* This compound has been suggested as a therapeutic agent in multiple myeloma.[24] Relief of pain has promptly followed administration of it in some cases but the progress of the disease goes inexorably onward. The facial anesthesia which often follows a full course of therapy with this non-heavy metal compound is a deterrent to its wider palliative use.

SUMMARY

1. The early localized lesion of a lymphoma which shows no evidence of spread to other areas is best treated by wide surgical excision followed by maximum intensive x-ray irradiation.

2. Total body irradiation appears to be the treatment of choice for chronic myelogenous leukemia in most instances. Radioactive phosphorus (P^{32}) is as effective, but the current difficulty of obtaining and handling the material limits its use to research institutions. Other radioactive elements as therapeutic agents at this time are neither as effective nor as practical for use as x-ray irradiation in treating neoplastic disease of the lymphoma group.

3. There has been no authenticated cure of any of the lymphomas and leukemias through treatment with any of the many chemotherapeutic agents tried in the past 20 years.

4. The nitrogen mustards have been shown to arrest the course of Hodgkin's disease in the majority of cases, but the change is temporary. In general, patients with Hodgkin's disease who have had no previous therapy have responded better and for longer remissions than those who have had x-ray therapy and are no longer responding favorably.

5. Urethane will alter the course of chronic myelogenous leukemia favorably, but the change is transient, and no permanent benefit has resulted in any case.

6. The mycosis fungoides and neoplastic disease of the giant follicular lymphoma group also respond favorably to the nitrogen mustards, the response being similar to that noted in the Hodgkin's disease group. The nitrogen mustards are a valuable adjunct to x-ray therapy in the treatment of Hodgkin's disease, mycosis fungoides and giant follicular lymphoma.

7. The remainder of the lymphomas and leukemias have shown transient response to the nitrogen mustards but in a much smaller percentage of patients.

8. Folic acid derivatives, such as pteroyldiglutamic acid and pteroyltriglutamic acid, are as yet unproven as effective palliative agents in any of the lymphomas and leukemias.

9. The administration of a folic acid antagonist, 4-aminopteroylglutamic acid, has been followed by temporary remissions in some cases of acute leukemia in children. There is no basis at this time for considering this compound as more than an arresting agent in some cases.

10. Many other agents are being actively investigated for their effect upon neoplastic diseases. None of these, however, can be recommended for general use as yet.

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California Cancer Commission Studies*
Chapter XXIII

Cancer of the Kidney and Testicle

FRANK HINMAN, M.D., *San Francisco*

A. CANCER OF THE KIDNEY

ALMOST all new growths of the kidney are malignant. Early diagnosis, before metastases occur, is necessary and must be followed by nephrectomy for a cure. In practice, fulfilment of the requirement of early diagnosis is the exception, for the clinical manifestations of neoplasm are absent, confused or indefinite. No precancerous manifestations or characteristic early symptoms are known. Death may result without any clinical indications of renal involvement.

Pathology: Renal tumors may be either parenchymal or pelvic in origin and position, and determining the type and degree of malignancy is of value mainly for prognosis, since the treatment for both is nephrectomy.

Primary neoplasms of the renal pelvis and calyces, which make up about 5 to 10 per cent of tumors of the kidney, are similar pathologically to tumors of the bladder. They are for the most part papillomatous, although those of squamous-cell types are much more common than in the bladder. The parenchymal tumors are two distinct types according to the age period of occurrence. The rapidly developing, highly malignant embryonal tumor (the adenomyxosarcomatous type of Wilms) of infancy is different pathologically from the common adeno- and alveolar carcinomata and the rare adenoma, cystadenoma and hypernephroma of adults, which usually occur between 40 and 50 years of age. (Figure 1.)

The papillary and squamous-cell tumors of the pelvis or calyces spread locally or by implantation as a rule, less often through the lymphatics and rarely through the blood stream.

The parenchymal tumors metastasize usually by way of the blood to any part of the body but most commonly to the lungs and long bones, a neoplastic fracture sometimes being the first indication of renal cancer. Lymphatic extension to the regional lymph nodes also occurs and this zone must be resected as cleanly as possible at the time of nephrectomy.

Symptoms: There are no pathognomonic symptoms in tumors of the pelvis and calyces. Hematuria is the most common symptom and usually is intermittent. The renal outline and function are usually normal in early stages of the disease, and the diagnosis of pelvic papilloma may be missed for many years. The filling defect on pyelography gives the most characteristic evidence, but the pyelogram may be normal. Patients with extension to the ureter and bladder as a rule present less difficulty in diagnosis. Ureteral catheterization may be impossible. Fragments of tumor in the urine, particularly after catheterization of the ureters, sometimes are found, and newer cytological studies of urinary sediment after the method of Papanicolaou may result in correct diagnosis.

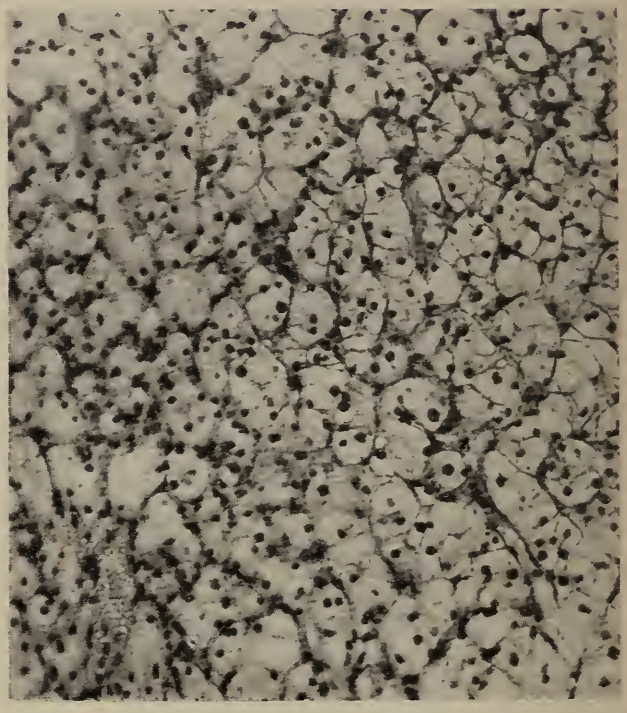


Figure 1.—Photomicrograph of a typical adenocarcinoma of the kidney superficially resembling adrenal cells, "clear undifferentiated foamy appearing cells." (After Judd and Hand, Arch. Int. Med., 44:746, 1929.)

The classical symptoms and signs of renal neoplasm are hematuria, pain and tumor. These are also common symptoms of other renal lesions and are never pathognomonic. While they are the cardinal symptoms of renal tumor, a diagnosis based on the presence of all three cannot be considered an early diagnosis. Although the duration and completeness of symptoms is no index of the degree of malignancy, the probability of metastases increases with the duration of symptoms. An early diagnosis is one which identifies the initial symptoms. *Hematuria is the initial symptom in about 40 per cent of cases, pain in 30 per cent and tumor in 10 per cent,* but in an analysis of some 1000 cases collected from various authoritative sources, at least one-third of the patients

*Organized by the Editorial Committee of the California Cancer Commission.

had all the cardinal trio at the time of operation (and presumably at the time of diagnosis also), whereas fewer than 100 had bleeding or pain or tumor alone. More than one symptom is uncommon at the onset, so that, from the clinical standpoint, an early diagnosis was missed in over 90 per cent of the cases.

Hematuria, renal pain or lumbar tumor has its chief importance in diagnosis as constituting the indication for complete investigation. The hematuria is neither continuous nor profuse. In only one of 146 cases of hematuria in renal neoplasm observed by Devaclara, did the attack last as long as 14 days. Hematuria is so common with other urogenital abnormalities that judgment of a high order is needed in deciding when it indicates the need of complete investigation. Sources in the lower tract (urethra, prostate, bladder) are commonest and when bleeding is not of a type indicating these sources, investigation of the upper tract is in order. *A safe rule is to determine the source of hematuria in every case,* even if of only a few hours' duration; and when the results of routine steps of a study of the lower tract are negative and the bleeding has occurred neither at beginning nor end of urination but the blood is uniformly mixed in the urine, there should be no hesitation in completion of the retrograde study of the upper tract.

Diagnosis: The most interesting diagnosis in the field of urology, which is notable for accuracy in diagnosis, is that of renal tumor. The diagnostic problem contains three parts for consideration: (1) The clinical evidence, (2) The urological findings, (3) the correlation of the two.

The filling defects of ureteropyelography may be the result of blood clots, inflammatory granulomas or pyelitis (and ureteritis) cystica. In primary papillary epithelioma of the ureter, which is very rare, the defect in filling is confined to the ureter, but the primary growth in the pelvis may be so small as not to cause a filling defect in the pyelogram. Differentiation has no practical importance since ureteronephrectomy is indicated for both.

The clinical differentiation of the different pathological types of parenchymal neoplasms is impossible. The mere diagnosis of tumor, if at all early, is noteworthy. Almost all tumors are unilateral and malignant. With the opposite kidney known to be present and healthy, *nephrectomy is the treatment for all growths* and clinical differentiation would have little value. The pathological differences, however, account for the considerable difference in the degree of malignancy, and an understanding of the gross microscopic and metastatic characteristics of the great variety of renal tumors is as necessary to the surgeon as to the pathologist.

Treatment: The sole treatment of renal tumor is nephrectomy which, to be curative, depends on early and accurate diagnosis. The growth must be removed completely before metastasis has occurred.

The use of x-ray therapy has not been shown to improve the prognosis, except that it may give considerable relief of pain in advanced cases. No cures are recorded except in Wilms' tumors. Preoperative irradiation may reduce the size of the tumor, particularly a tumor of the Wilms type, and thus facilitate nephrectomy.

B. CANCER OF THE TESTICLE

The knowledge of tumors of the testis has changed considerably. We now know that they are among the most malignant of all cancers, that they commonly occur in the most active period of reproductive life, between the ages of 20 and 40, that the onset is insidious and painless and that early recognition in the majority of cases is made by palpation of an indurated area inside the testis. So rare in this site are tumors of the benign types (adenoma, fibroma, myoma and others) that it is practical to regard all tumors of the testes as malignant. *Clinical differentiation is impossible and biopsy is altogether too dangerous since removal of a specimen materially lowers the chance of cure if the lesion is malignant.*

We now know that certain kinds of tumors are radiosensitive and that other kinds are radioresistant, while yet others are radiosensitive but not radiocurable.

It has long been known that removal of the testis before tumor cells have spread elsewhere by blood or lymphatics will effect a cure but, although the primary lymph zone of the testis was determined long ago and lymphatic extension was found to be the earliest and most common route of metastasis, the surgical principle so generally applied to cancer elsewhere, namely, complete removal of the tumor and its primary lymph zone, has not been popular. The reason for this is the apparent formidability of radical surgery and the fact that sometimes some of these tumors can be cured by x-ray therapy. However, as the radical operation has been found to be fairly simple compared to similar operations for other cancers and to have an almost negligible surgical mortality, it is still the logical procedure for all radioresistant tumors. Deciding just what tumors are radioresistant is the big problem. The accumulated correlation of the testicular pathology with the subsequent gradings of x-ray sensitivity or resistance of the metastases help in making this decision. As previously stated, however, the tumor in the testis may be at a radiosensitive stage while the subsequent transitions of the metastases may be radioresistant. This uncertainty and the logic of the surgical principle of early radical removal of any cancer has led a few urologists to practice early orchiectomy and resection of the preaortic lymph zone for all these tumors. The operative risk is well below 1 per cent—so low as fully to justify their point of view.

Pathology: In earlier pathologic studies homologous or monocellular growths were distinguished from heterologous or multicellular growths and in each group certain types were defined. This dual classification with its subdivisions proved most unsatisfactory. Now and then a tumor appeared which did not fit into any part of the classification. It was Ewing who suggested that all testicular tumors, with

the obvious few exceptions, arose from a totipotential cell. Recent clinical observations confirm this view.

The most accepted classification today is that of the Army Institute of Pathology (Friedman and Moore, 1946): (1) Seminoma (germinoma); (2) Embryonal carcinoma including chorioepithelioma (Figures 3 and 4); (3) Teratoma (Figure 5); (4) Teratocarcinoma.

It is felt that all of these tumors arise from a totipotent sex cell, and that teratomas and teratocarcinomas probably arise through differentiation of embryonal carcinoma, hence expressing the latent potentialities of the embryonic germ cells.

Diagnosis: As a rule the patient finds something unusual ("a lump") in his testicle, for which he consults a doctor. Since these patients are young men, most of whom have never given cancer a thought, it is not surprising that this consultation too frequently is delayed, long enough to be fatal. Men can be taught the significance of a hard spot in the testis just as women have been about cancer of the breast, and an increase in the number of early diagnoses will save many lives. Accidental discovery during a routine physical examination also occurs, as was the case in the last war when large numbers of young men were examined.

Clinical diagnosis is made by palpation (except in the rare instances of a high content of hormone in the urine with negative findings on palpation). Ordinarily the testicle and its epididymis are distinguishable. In small growths an area of induration can be made out, but in larger growths the general shape of the testicle, as a rule, is maintained as in gumma. The examiner receives the impression, however, of an increase in weight or perhaps more nearly an increase in the specific gravity of the enlarged testicle. As a rule the surface is smooth, rarely is there nodulation (such as is caused by tuberculosis, strangulation of a hydatid, chronic infection). Even in advanced growths the epididymis can still be separated from the mass and difficulties in differential diagnosis usually arise only when this becomes impossible because of coexistent hydrocele or epididymitis. Careful search for metastases should always be made. The earliest site of metastasis is the preaortic lymph zone, but metastasis to the supraclavicular group of glands called "Virchow's node" is not at all infrequent. Metastasis also occurs to the viscera by way of the blood vessels. It is, of course, important to determine at the time of examination the presence and the extent, or the absence of any of these kinds of metastasis.

For some time now it has been known that certain of these embryonal tumors secrete a gonadotropic hormone which is excreted by the kidneys much as a similar hormone is

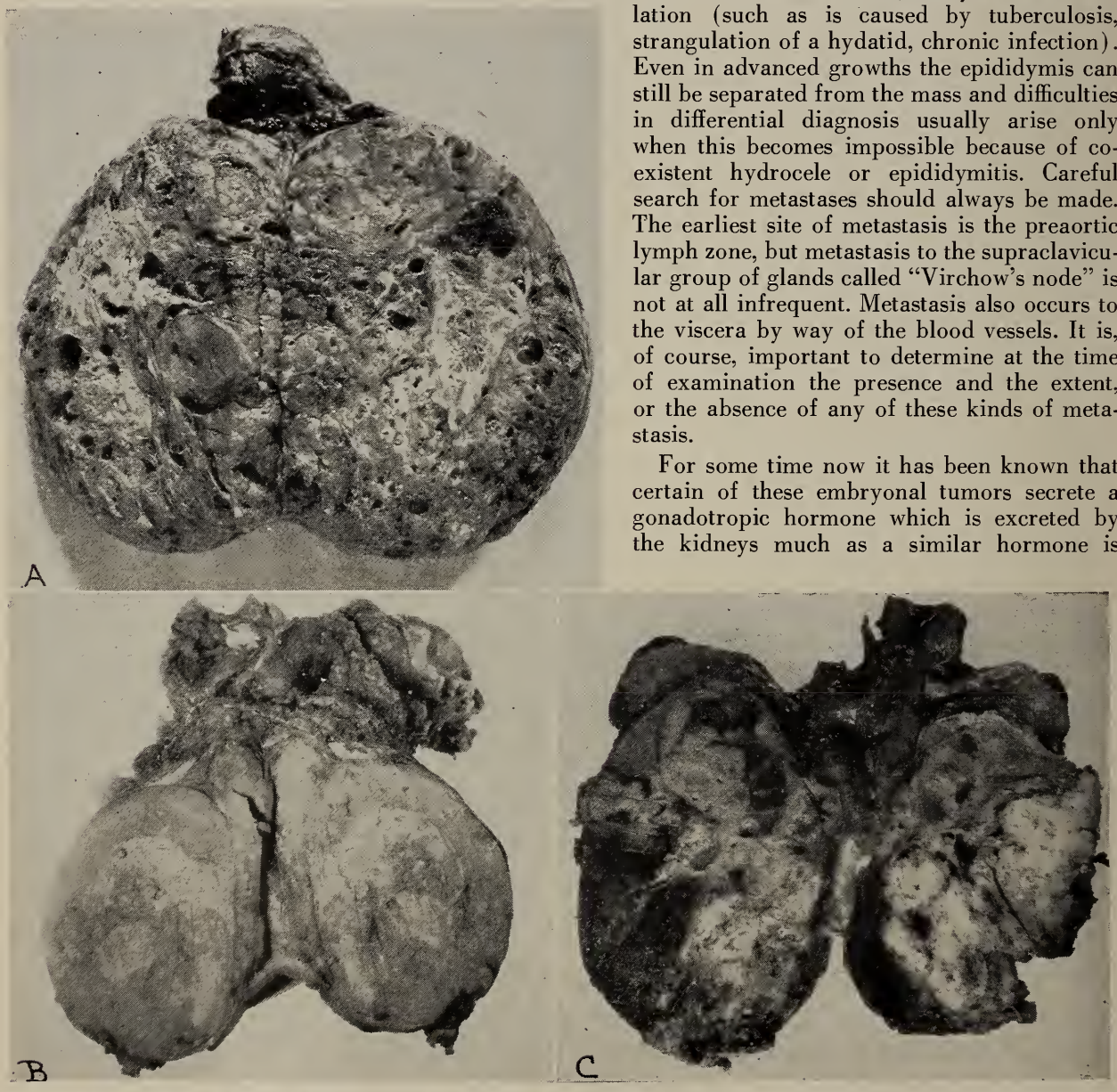


Figure 2.—Photographs of the gross appearance on cross section of specimens removed by orchiectomy. (A) Embryonal teratoma. (Hinman, F: The principles and practice of urology, 1935). (B) Seminoma. (C) Chorionepithelioma.

during pregnancy. It seems that the hormone (gonadotropin) is formed only by chorionic-like cells. Hence a strongly positive result in an Aschheim-Zondek test (10,000 rat units) signifies a chorionepithelioma, while a slightly positive result indicates a potential chorionepithelioma. The result is negative, however, if the testicular cancer is of another type, and therefore *a negative result does not rule out malignancy.* Several workers have had the experience of finding an apparently pure embryonal carcinoma or adenocarcinoma in the removed testis of a young man with negative reaction to the Aschheim-Zondek test, the result of later tests then becoming strongly positive within a matter of months, with a rampant chorionepithelioma found in the metastases at autopsy. Nevertheless, the test remains useful.

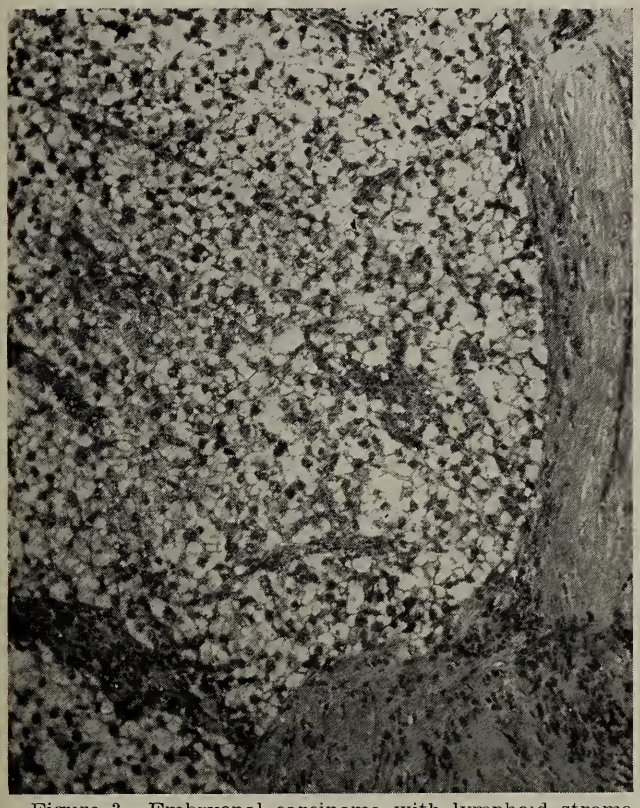


Figure 3.—Embryonal carcinoma with lymphoid stroma just developing. Small round cells lying in a light reticulum. (From Hinman, F. and Smith, D. R.: The testicles and epididymes, In: Oxford Loose Leaf Urology, 1942, Figure 16.)



Figure 4.—Typical chorionepithelioma. (From Hinman, F. and Smith, D. R.: The testicles and epididymes, In: Oxford Loose Leaf Urology, 1942, Figure 22c.)

Treatment: Treatment is not uniform and too much reliance is put on radiation. Diagnosis at the earliest possible opportunity comes first. This can only be done by an immediate orchiectomy upon discovery of a nodule in a testicle. The author can see no benefit to be gained by preoperative irradiation which carries with it a risk of sterilization even with the best of lead protection of the good testis. With exposure of the cord at the external ring and double ligation and division before manipulation of the tumor, orchiectomy would seem to be perfectly free from danger of causing metastases. It is advisable to have collected urine for 24 hours or more before castration for determination of the gonadotropic hormone. There is no advantage in waiting for the result of this test, however, before performing orchiectomy inasmuch as neither the presence nor the absence of the hormone would modify the immediate treatment. The specimen removed is sent to the pathologist for careful serial examination and this study together with the report from the biochemical laboratory will guide future management. Resection of the preaor-



Figure 5.—Tridermal elements of adult teratoma, nonmalignant. Note cartilage, simple cysts, gastrointestinal epithelium, tooth buds, nerve tissue and other mesenchymal cells. (From Hinman, F. and Smith, D. R.: The testicles and epididymes, In: Oxford Loose Leaf Urology, 1942, Figure 15.)

tic lymph zone may be performed on all patients who show no evidence of metastasis, except those with seminoma who receive, instead, 1,000 r of deep x-ray therapy to this zone. The results of radical operation in a large unselected group (Lewis, 1948) indicate its value in all tumors except seminomas. Simple orchiectomy will cure early tumors in patients without metastases. In practice, early diagnosis and orchiectomy are always indicated, and surgical resection of the preaortic lymph zone is justified when subsequent pathologic studies indicate that the tumor is radioresistant and inoperable metastases are not demonstrable.

When the diagnosis is late and metastases are evident, the prognosis is poor unless the growth is radiosensitive. Even then, surgical removal of isolated metastatic nodules, preaortic and supraclavicular, may be indicated as adjuncts to deep x-ray.

SUMMARY: CANCER OF THE KIDNEY

1. Hematuria is the initial symptom in 40 per cent of the cases of cancer of the kidney; hematuria should mean carcinoma until ruled out.
2. Hematuria, pain and tumor together mean a late stage of the disease and probable incurability.
3. Treatment is nephrectomy; x-ray is useful only for relief of pain.

SUMMARY: CANCER OF THE TESTICLE

1. The frequency of testicular neoplasm must be made clear to young men so that they may be treated early.
2. Orchiectomy is necessary in all cases, for diagnosis and determination of subsequent therapy.
3. Seminomas are treated with orchiectomy and x-ray while for other tumors the treatment is orchiectomy and radical lymph node dissection. Large doses of x-ray are used in patients with inoperable metastases.

"Cancer of the Breast," by Alson R. Kilgore, M.D., Chapter XVIII of the California Cancer Commission Studies, will be published in this section of the November issue of CALIFORNIA MEDICINE.

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Editor, DWIGHT L. WILBUR, M.D. *Assistant to the Editor*, ROBERT F. EDWARDS

Editorial Executive Committee

LAMBERT B. COBLENTZ, M.D., San Francisco ALBERT J. SCHOLL, M.D., Los Angeles
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EDITORIAL

November 2, 1948

Californians will have a chance, along with the rest of the nation, to cast their ballots on November 2 on the pros and cons of candidates and issues. The ballot in this state will be a long one, due to the presence of 19 propositions which have been placed before the electorate under the initiative and referendum laws of the state.

Heading the list on the ballot will be the candidates for President of the United States, with Harry S. Truman and Thomas E. Dewey vying for top honors. (Henry Wallace, the Communist candidate, the Dixiecrat candidate and others need no further consideration here.) Mr. Truman has consistently echoed the late FDR's sentiments concerning a system of state medicine; Mr. Dewey has been positive and strong in his assertions that a system of private medical practice is better and more beneficial to the people than a government-controlled system. Doctors may make their own choice between the two.

Next come the candidates for Congress and the State Legislature and in some districts there will be hot contests. The California Medical Association makes it a policy not to sponsor individual candidates but there is no avoiding the preference which physicians are likely to show for one or another contestant because of his views on the private enterprise system or a firmly-controlled system of governmental paternalism and professional slavery. The doctors in each district are aware of the proclivities of their own candidates and will vote accordingly.

State propositions will follow the list of candidates for office. There will be 19 of these and there would have been 20 if the State Supreme Court had not voted unanimously last month to throw out the so-called "Omnibus" or "Bill of Rights" initiative. This bill would have amended 15 of the 25 articles of the State Constitution, a fact which the Supreme Court held to be a virtual revision of the Constitution. Such revision is permitted only by a Constitutional Convention. The bill would, among other things, have placed the licensing and control of all the healing arts professions under a board of five "naturopathic physicians," a quaint term for a chiropractor who wishes to gain a new title and new authority by passing a law. The potential spectacle of a board of five chiropractors passing on the professional qualifications of doctors of medicine was not overlooked by the Supreme Court. The justices, by unanimous vote, decided that this issue was not to go before the voters; in so doing they eliminated what promised to be a tough fight for the physicians and for all other business and professional interests in the state, a fight for right and justice against the emotionalism engendered in special interest groups of old-age pensioners, partly-trained professional men, professional sob-sisters and others whose legislative programs have failed of accomplishment before the tribunal of the State Legislature.

Of the remaining ballot propositions, Number 4 and Number 13 appear to be of greatest interest to physicians. Number 4 is the so-called "McLain Bill" to increase pensions to the aged, to control the payments of assistance to the blind and to provide a different system of hospitalization for recipients of state aid. The bill would alter the present system of medical care in county hospitals, would permit various practitioners to serve on county hospital staffs and would permit the acceptance of many cases by county hospitals regardless of the ability of the patient to pay for his own care. The California Medical Asso-

ciation has gone on record as opposing this measure. If the professional angles of this bill are not enough, let the doctor remember that state taxes would be increased $135,000,000 the first year under this bill and an eventual $235,000,000 as the plan progressed. Even these estimates might be too low if a flood of potential old-age assistance recipients from other states came to California, drawn by the magnet of something for nothing.

Proposition Number 13 has not been acted upon officially by the Association, but the sentiment of most doctors seems to be against it. This bill would bring about a reapportionment in the State Senate, basing Senate representation on a population basis instead of an area basis, as at present. The four most populous counties would have 21 senators under the proposals of this bill, as compared with four at present. Conversely, the rural counties of the state would lose their Senate representation. The State Legislature would be composed of 48 assemblymen from four counties, out of a total of 80 assemblymen, and 21 senators from these same counties out of a total of 40. If the rural areas are to retain any vestige of a voice in the Legislature, and if the system of checks and balances now existing in the Federal and in state government is to be maintained for the State of California, this bill will be defeated. If this is done, California will continue to operate on the same basis as the Federal Government, where the House of Representatives is apportioned on a population basis and the Senate on an area basis.

As a matter of policy the California Medical Association refrains from entering into any controversial legislative or elective issue except where the art or practice of medicine is directly concerned. The remarks made here are in line with this policy, and the actions of the Council and legislative committee of the Association bear out the same thought. On the other hand, the Association retains its right to suggest fundamental concepts in the exercise of individual rights in a free election. Two such basic principles which suffer not at all from reiteration, occur at this moment. First, know your candidates and your ballot propositions and decide which side you wish to support. Second, and more important, get out on November 2, 1948, and VOTE.



Letters to the Editor . . .

San Diego

Editor, California Medicine

Dear Sir:

I am keenly interested in the thought behind your recent editorial in California Medicine on the "easy bruiser" and medical care plans. I am thoroughly convinced that it is high time the physician members of C.P.S. define more exactly than has been done, up to the present time, the nature of the obligation which the physician assumes in respect to the cost of medical care.

I would like to submit for your consideration the following definition of this obligation:

Organized medicine (defined as ethical private practitioners of medicine) should assume the obligation of making provision for all non-indigent citizens who give medical service a high priority expense rating, an opportunity to obtain private medical care of high quality. For those citizens of limited income all encouragement should be given to commercial plans and all effort should be made through C.P.S. policies to accomplish the above-stated goal. In order to avoid the inevitable abuses which will result in excessive premiums or inferior quality of medical care, the insured individuals should be required to pay directly to the physician part of the expense of all medical service received.

To effectuate such a policy two devices may be used. First, through indemnification the insured may receive a stated amount for particular services. The insured will pay the difference between this amount and the fee charged. The second method would be for the insured to pay a stated amount and/or per cent of the fee, and the balance covered by the insurance. Extension of insurance coverage to minor conditions will, I am sure, lead to constantly increasing premiums or the alternative of constantly decreasing quality of care received. I would, personally, like to see C.P.S. investigate the possibility of selling a policy competing with present C.P.S. policies incorporating the above ideas. I would be surprised if such competing policy would not find itself in an ever increasing position of strength in relation to the present type coverage. Its strength would lie in the fact that it does not remove personal financial responsibility from the insured. Personally I would favor the per cent rather than the fixed amount of deductibility. A two-thirds/one-third division between insurance and responsibility would appeal to me.

Before closing I would like to state further that I have noted a continuous and ever-increasing tendency on the part of persons insured under the Blue Cross Hospitalization plan to ever-increasing use of this insurance. I feel that the same competing type of hospitalization policy is worthy of trial. Here, again, I would suggest something in the nature of a two-thirds/one-third division after, let us say, the first $25.00 of hospitalization expense.

Sincerely yours,

William C. Black, M.D.

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JOHN HUNTON, Executive Secretary.....General Office, 450 Sutter Street, San Francisco 8
ED CLANCY, Field Secretary.....Southern California Office, 417 South Hill Street, Los Angeles 13

NOTICES AND REPORTS

New California Medical Association Constitution and By-Laws

The following is a tentative draft of a proposed revision of the Constitution and By-Laws of the California Medical Association. Work on the revision was undertaken first by a committee of 16 authorized by the 1947 House of Delegates to review the existing document. That committee's draft was referred to a committee of five by the 1948 House of Delegates for further study.

Comments and suggestions by C.M.A. members, which are solicited by the committee, should be addressed: Committee on Constitution and By-Laws, Sam J. McClendon, M.D., chairman, California Medical Association, 450 Sutter Street, San Francisco 8.

CONSTITUTION

ARTICLE I.—NAME, PURPOSES AND ORGANIZATION

Section 1.—Name

The name of this organization is California Medical Association (hereinafter referred to as the Association).

Section 2.—Purposes

The purposes of this Association are to promote the science and art of medicine, the protection of public health, and the betterment of the medical profession; to promote similar interests of its component societies; and to unite with similar organizations in other states and territories of the United States to form the American Medical Association.

Section 3.—Organization

This Association has two divisions: One, the Association as an organization; and Two, the Scientific Assembly. The Association as an organization includes component societies and their active members, the House of Delegates, Council, Commissions and Standing Committees. The Scientific Assembly includes all members of the Association and the scientific sections.

Section 4.—Definition of Component Societies

Component societies include all county medical societies (which may cover one or more counties) heretofore or hereafter chartered by this Association.

Section 5.—Component Society Charters

Charters to component societies may be granted and revoked as hereinafter prescribed, subject to the limitation that only one charter may be outstanding at any one time in any county.

ARTICLE II.—MEMBERSHIP

Section 1.—Classes of Members

The members of this Association shall consist of Active, Associate, Honorary, Retired, Life and Affiliate members.

Section 2.—Membership Qualifications, Rights, Privileges, Duties and Method of Election

The qualifications, rights, privileges, duties, obligations and methods of election of the several classes of membership are as stated in the By-Laws.

County Society Secretaries' Conference

A conference of secretaries of the component medical societies of the California Medical Association, the first since the entrance of the United States into the war, will be held February 4 and 5, 1949, in San Francisco. Formerly such conferences were held annually. Date for the 1949 conference was set by the Executive Committee of C.M.A. at a meeting in August.

ARTICLE III.—GOVERNMENT OF THE ASSOCIATION

Part A.—House of Delegates

Section 1.—Composition

The House of Delegates shall consist of:

(a) Delegates elected by the members of component societies; and

(b) Officers of the Association as hereinafter provided.

Section 2.—Representation

As the By-Laws shall provide, each component society shall be entitled to proportionate representation in the House of Delegates but with a minimum of one delegate.

Section 3.—Alternates

One or more alternates shall be elected for each delegate in the same manner as delegates are elected. One alternate shall be seated in place of each delegate absent or disqualified for failure to attend meetings or other cause.

Section 4.—Terms of Delegates and Alternates

Delegates and alternates shall serve for three years. One third, as nearly as possible, of the allowed number shall be elected each year.

Section 5.—Quorum

A majority of the authorized number of delegates shall constitute a quorum.

Section 6.—Functions of the House of Delegates

The House of Delegates shall be the legislative body of the Association and, in addition, shall exercise such other functions as the By-Laws may prescribe.

Section 7.—Issuance and Revocation of Charters

(a) The House of Delegates shall issue charters to medical societies of a county or combination of counties deemed eligible and having made proper application therefor.

(b) The House of Delegates may suspend or revoke any such charter, after due notice and proper hearing, for cause. "Cause" shall be considered to be any conduct or action, on the part of any component society, deemed in contravention of the Constitution and By-Laws of the Association or the American Medical Association or its "Principles of Medical Ethics." "Cause" shall further be deemed to be any conduct or action of a component society deemed inimical to the best interests of the Association.

(c) It may act on the withdrawal or secession of any component society from the Association and take such measures as are deemed advisable and proper for reinstatement of any component society which may have withdrawn or had its charter suspended or revoked.

(d) A two-third affirmative vote of the delegates present and voting shall be necessary for any action under the provisions of this section.

Section 8.—Sessions of the House of Delegates

In each year there shall be one or more regular sessions of the House of Delegates as fixed in the By-Laws. Special sessions may be called and held as provided in the By-Laws.

Part B.—Council

Section 9.—Composition

The Council shall consist of:

(a) One Councilor, elected from each district; and

(b) The President and President-Elect of the Association.

In addition, the Speaker, Vice-Speaker, Secretary-Treasurer, and Editor, all ex-officio but without the right to vote.

Section 10.—Councilor Districts

There are fifteen councilor districts as follows:

District Number One, comprising San Diego and Imperial counties.

District Number Two, comprising Orange, Riverside and San Bernardino counties.

District Number Three, comprising that area included in the 1937 city limits of the City of Los Angeles and now (1948) known as Councilor District No. 1 (g) of the Los Angeles County Medical Association.

District Number Four, comprising the balance of Los Angeles County except as stated in District Number Three, now known (1948) as Councilor District No. 2 to No. 7, inclusive, of the Los Angeles County Medical Association.

District Number Five, comprising Ventura, Santa Barbara and San Luis Obispo counties.

District Number Six, comprising Monterey, San Benito and Santa Cruz counties.

District Number Seven, comprising Santa Clara and San Mateo counties.

District Number Eight, comprising San Francisco County.

District Number Nine, comprising Alameda and Contra Costa counties.

District Number Ten, comprising Kern, Kings, Tulare, Inyo, Mono, Madera and Fresno counties.

District Number Eleven, comprising Merced, Mariposa, Stanislaus, Tuolumne, Alpine, Calaveras and San Joaquin counties.

District Number Twelve, comprising Sacramento, Amador, Eldorado, Placer, Nevada, Sierra, Yuba, Sutter, Yolo, Colusa, Glenn and Butte counties.

District Number Thirteen, comprising Plumas, Tehama, Shasta, Lassen and Modoc counties.

District Number Fourteen, comprising Siskiyou, Del Norte, Humboldt, Trinity, Mendocino and Lake counties.

District Number Fifteen, comprising Sonoma, Napa, Solano and Marin counties.

Section 11.—Election of Councilors

Councilors shall be elected by vote of the delegates within each district in the manner and at the time specified in the By-Laws.

Section 12.—Councilors: Terms of Office

Councilors shall serve for terms of three (3) years; one-third to be elected in each year.

Section 13.—Council: Powers and Duties

Subject to the provisions of this Constitution, and all resolutions and enactments of the House of Delegates, the Council shall be vested with full and complete power and authority to manage, control, use, invest, reinvest, lease, make contracts in respect of, and concerning, convey, give, grant, transfer or otherwise dispose of all property and assets of whatever kind or nature owned by the Association, and shall also be vested with full and complete power and authority to do and perform all acts and to transact all business for and on behalf of the Association and to manage and conduct all the work and activities of the Association in carrying out the purposes thereof. The Council shall have such additional duties, powers and functions as are prescribed in the By-Laws.

Section 14.—Election of Councilors on Adoption of this Constitution

Upon the adoption of this Constitution, the delegates from each district shall proceed to elect Councilors as follows: At the annual meeting at which this Constitution is adopted, the Councilors of the First, Fourth, Seventh, Tenth and Thirteenth Districts shall be elected for terms of one year each; Councilors of the Second, Fifth, Eighth, Eleventh and Fourteenth Districts shall be elected for terms of two years each; and Councilors of the Third, Sixth, Ninth, Twelfth and Fifteenth Districts shall be elected for terms of three years each. Thereafter, as each term expires, the delegates from the districts shall elect a Councilor to serve for a term of three years.

Upon the adoption of this Constitution and the election of fifteen district Councilors, as above provided, the terms of office of the Councilors elected prior to the adoption of this Constitution shall immediately cease and terminate.

ARTICLE IV.—FUNDS, PROPERTY, DUES, ASSESSMENTS AND EXPENDITURES

Section 1.—Annual Dues

At each regular session the House of Delegates shall, by a majority vote, fix the annual dues to be paid by members of the Association for the ensuing calendar year. Dues payable by active members shall be uniform and equal, except that the House of Delegates may reduce dues for certain groups (by general classification) as the By-Laws may expressly permit.

Dues payable by associate members shall be uniform and equal but may be set at not less than one half the regular dues for active members.

Section 2.—Military Service

During any period at which the United States is at war or requires services of doctors of medicine under an universal military training program, annual dues may be reduced or waived by the House of Delegates with respect to those members serving in the Armed Forces of the United States during the whole or any part of any year.

Section 3.—Leaves of Absence

The Council, on recommendation of a component society, may grant leaves of absence to active members who are seriously ill and cannot practice or who leave practice temporarily for postgraduate study or other purposes acceptable to the component society and the Council and during such leave no dues shall be payable; provided no leave may exceed one year.

Section 4.—Special Assessments, etc.

Funds may also be raised by any of the following methods: (a) publications of the Association; (b) voluntary contributions; (c) bequests, legacies, devises, and gifts; (d) special assessments levied by the House of Delegates; and (e) in any other manner approved by the House of Delegates. In the event that the House of Delegates levies any special or other assessment than the annual assessment of dues, it may, in the resolution levying the assessment, fix and determine the time within which such assessment must be paid, the class or classes of members of the Association upon whom it is levied, and the penalty, if any, including forfeiture or suspension of membership in this Association or the component society, or both, to result from nonpayment thereof within the time prescribed.

Section 5.—Annual Budget and Expenditures

At each regular session of the House of Delegates, the Council shall submit to it an itemized budget stating the proposed expenditures of the Association for the ensuing year. The budget shall contain a contingency fund not exceeding the amount specified in the By-Laws, such fund to be available for expenditure at the discretion of the Council. The budget may be altered or revised by the House of Delegates, but must be adopted by the House before adjournment of the session. After its adoption, no expenditures in excess of the amount of the budget item covering the subject of such expenditures may be made in the year covered by the budget by the Association or any of its officers, agents or employees, unless the House of Delegates shall first approve such excess expenditure by resolution duly adopted. Recurring items in the budget (fixed expenditures covering more than one year), shall, when first adopted, be binding as to subsequent budgets to the extent of commitments or obligations entered into by the Association within authority granted by the House of Delegates or this Constitution or the By-Laws.

Section 6.—Benevolence Fund

At least $1.00 out of the annual dues paid by each member of the Association shall be allocated to the Physicians' Benevolence Fund and shall only be used for the purposes as set forth in the By-Laws.

Section 7.—All Funds and Moneys to Be Paid to Secretary-Treasurer and Deposited With Depositary

All funds and moneys received for the Association by any officer or agent thereof shall be promptly paid to the Secretary-Treasurer and by him deposited with a depositary selected as such by the Council.

All depositaries selected by the Council shall be banks or trust companies duly licensed to transact business as such in the State of California.

Section 8.—Membership Interest in Association Property

No person other than an active member in good standing shall have any interest in the property of the Association and the interest of any active member therein shall cease when he ceases to be a member of the Association.

If any active member shall resign or otherwise cease to be an active member of the Association, all of his interest in and to all property of the Association shall cease and such cessation of membership shall operate as a release and assignment to the Association of all the right, title and interest of such member in and to all the property of the Association.

ARTICLE V.—REFERENDUM AND PETITION

Section 1.—Referendum and Petition

The right of referendum and petition shall be as set forth in the By-Laws.

ARTICLE VI.—OFFICERS

Section 1.—Officers

The officers of this Association shall be a President, a President-Elect, a Secretary-Treasurer, a Speaker of the House of Delegates, a Vice-Speaker of the House of Delegates, an Editor and fifteen Councilors.

Section 2.—Powers and Duties of the President-Elect

The President-Elect shall act for the President in his absence or disability, and if the office of President becomes vacant the President-Elect shall then succeed to the Presidency to serve as President for such unexpired term and for the term of one year thereafter.

ARTICLE VII.—SCIENTIFIC ASSEMBLY

Section 1.—Objects

The Scientific Assembly of the California Medical Association is the convocation of its members for the presentation and discussion of subjects pertaining to the science and art of medicine.

Section 2.—Sections

The Scientific Assembly shall be divided into sections, each section representing that branch of medicine described in its title.

Section 3.—Creation of New Sections

New sections may be created or existing sections discontinued by the House of Delegates. The Scientific Assembly and its sections shall be conducted in accordance with the provisions of this Constitution and the By-Laws, and such other instructions by the House of Delegates or the Council as may not be in conflict therewith.

ARTICLE VIII.—MISCELLANEOUS

Section 1.—Incorporation

(a) To aid in carrying out the objects of the Association, the House of Delegates at any meeting of any regular or special session thereof may by a two-thirds vote of the members thereof present and acting, authorize, empower and direct the Council to cause the formation and organization of a non-profit corporation under the laws of the State of California, without capital stock, with such incorporators, name, purposes, objects, principal place of business, term, number of directors and directors to serve for the first year and until their successors are elected and have accepted office, and with such provisions regarding the voting power and property rights and interests of the members of the corporation and such further provisions in the Articles of Incorporation thereof, and with By-Laws and composed of such members representing this Association as the Council shall prescribe, fix and determine. The House of Delegates may at its option in connection with the granting and giving of such authority, power and direction to the Council, prescribe, fix and determine any or all of such matters pertaining to the said corporation, its Articles of Incorporation and any provision thereof, By-Laws and membership, and its action thereon shall bind the Council; and the House of Delegates at any meeting of any regular or special session thereof may by a two-thirds vote of the members thereof present and acting, authorize, empower and direct the Council to grant, assign, transfer, convey and deliver, or cause to be granted, assigned, transferred, conveyed and delivered to the said corporation upon the formation thereof without any consideration therefor, any property, real or personal, of the Association, which authorization, power and direction may be given prior or subsequent to the formation and organization of said corporation.

(b) To further aid in carrying out the objects of the Association, the House of Delegates at any meeting at any regular or special session thereof may, by a two-thirds vote of the membership thereof present and acting, authorize, empower and direct the Council to cause the formation and organization of one or more corporations under the laws of the State of California with such incorporators, name, purposes, county where the principal office for the transaction of business is to be located, first directors, the total number of shares, the aggregate par value, if any, of all shares, classes of shares, par value of any shares having par value, statement of the provisions, privileges and restrictions granted or imposed upon the respective classes of shares, or if the corporation be formed without capital stock the authorized number and qualifications of its voting and other rights of each class of members and the liability of each and all classes, to dues or assessments, and with such further provisions in the articles of incorporation thereof and with such by-laws as the Council shall prescribe, fix and determine; and the House of Delegates at any meeting of any regular or special session thereof may, by a vote of two-thirds of the members thereof present and acting, authorize, empower and direct the Council to grant, assign, transfer, convey or deliver or cause to be granted, assigned, transferred, conveyed or delivered to any of such corporations upon the formation thereof or to applicants for health and

accident or other insurance in or from any of said corporations at or prior to the formation thereof without any consideration therefor, such funds and property, real or personal, of this Association as the House of Delegates shall from time to time authorize or ratify.

Section 2.—Seal

The Association shall have an Association seal consisting of a circle having on the circumference the words "California Medical Association, Eureka, 1856," with such further emblems, figures and words as the House of Delegates, on recommendation from the Council, shall prescribe.

The power to change the seal shall rest with the House of Delegates.

Section 3.—Amendments

Any member of the House of Delegates at any meeting of any regular annual session thereof may present an amendment or amendments to any article or articles or any section or sections of any article or articles of this Constitution.

Such proposed amendment or amendments shall be in writing and shall be filed with the Secretary and shall thereafter be published at least twice in separate issues of the official journal of this Association prior to the next regular session of the House of Delegates.

At the said next regular session of the House of Delegates, such proposed amendment or amendments shall be submitted to the House of Delegates, for consideration at any meeting of the House of Delegates during that annual session, and if two-thirds of the Delegates present and voting vote in favor thereof, the same shall be adopted.

Section 4.—Repeal of All Provisions of Existing Constitution

All articles and all sections and all parts of all articles of the existing Constitution are hereby repealed.

BY-LAWS

CHAPTER I.—COMPONENT SOCIETIES

Section 1.—Component Society Charters

The charter of each component society shall provide that all the provisions of the Constitution and By-Laws of this Association in force at the time of the issuance of such charter, together with all amendments to either thereof thereafter adopted, in so far as the same are applicable, shall be an integral part of the Constitution and By-Laws of the component society to which the charter is issued and that the terms and provisions thereof shall control and govern such component society, the officers and members thereof, and that the constitution and by-laws of the component society shall not be amended in any way to conflict or be inconsistent with the Constitution and By-Laws of this Association. Each charter shall be signed by the President and the Secretary-Treasurer of this Association.

Section 2.—Revocation of Component Society Charters

The charter of any component society may be revoked by the House of Delegates if, after the filing with the Secretary-Treasurer of this Association of a written petition or protest signed either by the Chairman of the Council pursuant to resolution adopted by the Council by the affirmative vote of two-thirds of all the members thereof, and after due notice of hearing and after hearing thereof, the House of Delegates by a two-thirds vote of its members decides that the provisions of the Constitution or By-Laws of this Association or of the charter of such society have been breached by such society or that such society has committed acts or conducted itself in conflict with the Constitution, By-Laws or purposes of this Association to such extent as to make such revocation desirable in the best interests of this Association.

Section 3.

(a) *Geographical or Specialty Sections.* A component society may authorize the formation and existence of branch geographical or specialty sections for scientific investigation and work only, and the members of such geographical sections or specialty sections must be members of such component society.

(b) *Members in Sections to Be Members of Respective Component Societies.* No geographical or specialty section shall be permitted to have any classes of members which classes in whole or in part include non-members of the component society of which any such geographical or specialty section is a branch or subdivision; provided that nothing in this section shall be construed as limiting the guest privileges of such non-members at meetings of such section.

Section 4.—Component Societies Exclusive Judges of Qualifications of Applicants for Membership

Each component society shall, subject to the minimum requirements for eligibility as provided by the Constitution, determine the qualifications for membership therein and shall be the sole judge of the qualifications of applicants for such membership.

A member must not practice or claim to practice, support, cooperate with or in any other way endorse any exclusive or sectarian system of medicine. He shall be honorable and ethical in his conduct and shall subscribe to the principles of medical ethics of the American Medical Association and to such as may from time to time be adopted by the California Medical Association, and shall recognize the authorized officers of his component society and of this Association as the proper authority to interpret any doubtful points in ethics.

Every applicant for membership in a component society shall fill out and sign in duplicate the application blanks provided by the society, which prescribe the necessary qualifications for membership. One copy of each such application shall be promptly forwarded to the office of this Association.

Section 5.—Component Society Rosters of Members and of Licensed Physicians in Counties

The Secretary of each component society shall keep a roster of its members and of the non-affiliated registered physicians of the county, on which shall be shown the full name, address, school and date of graduation, date of license to practice in this State and such other information as may be deemed necessary. In keeping such roster the component society's secretary shall note and at once notify the Secretary-Treasurer of this Association of any changes in the personnel of the profession, by death, by resignation, or by removal to or from the county, and in making his annual report he shall endeavor to account for every physician who has lived in the county during the year. The secretary of each component society shall make a monthly report to the Secretary-Treasurer of this Association upon such forms and including such subjects as are herein provided, and as the Council may authorize.

CHAPTER II.—MEMBERSHIP

Section 1.—What Constitutes Membership

The name of a doctor of medicine on the official roster of this Association, after it has been properly reported by the secretary of his component society, and after the dues or other assessments due this Association shall have been paid by the component society for each such member according to the class of membership held by each component society member, shall be prima facie evidence of membership, and of his right to register at the Annual Session.

Section 2.—Qualifications for Membership and Method of Election Thereto

(a) *Active Members.* Active members shall comprise all active members of all the component societies. No person shall be eligible for election to active membership in a component society unless he shall hold the degree of Doctor of Medicine issued to him by an institution of learning, accredited at the time of conferring such degree by the American Medical Association or the Association of American Medical Colleges. He must also hold an unrevoked license to practice medicine and surgery in the State of California; provided, however, that subject to the minimum qualifications prescribed by this Constitution and the By-Laws, each component society shall be the exclusive judge of the qualifications of the members thereof.

(b) *Associate Members.* Associate members may be elected by the Council, upon recommendation of the component societies of the counties in which the associate members reside, from those doctors of medicine engaged in teaching or research work or holding positions in the Federal Service or otherwise, and from other persons engaged in medical teaching or research or other scientific work contributing to medicine and the public health.

(c) *Retired Members.* Retired members shall be elected by the Council on the recommendation of any component society from those active members thereof who cease the practice of medicine for reasons satisfactory to such component society and the Council, and who shall have been active members of the Association for a total of ten years prior thereto.

(d) *Honorary Members.* The House of Delegates on recommendation by the Council may elect as honorary members any persons distinguished for their services or attainments as doctors of medicine or in the field of public health, or for research or other scientific work contributing to medicine.

(e) *Life Members.* Life members may be elected by the Council on the recommendation of any component society from those active members thereof who have been active members of this Association continuously for a period of twenty (20) years or more and are more than fifty years of age. Those active members over seventy years of age need not be recommended by any component society but are eligible to life membership on direct application to the Council. The Council may not elect to life membership any active member whose membership has not been continuous or who has ever been censured, suspended or expelled from the American Medical Association, this Association, any state medical association which is a constituent unit of the American Medical Association, or any county medical society which is a component part of this Association or a unit of any other state medical association.

(f) *Affiliate Members.* The House of Delegates may, from time to time, establish special and limited classes of membership in this Association for internes, junior and senior residents, or house officers, practicing in hospitals in this state. In establishing such special membership for internes, junior and senior residents, or house officers, the House of Delegates may determine the qualifications, duration and privileges of such membership. Unless the House of Delegates determines to the contrary, such special members shall not pay dues.

The House of Delegates may also from time to time provide for affiliation with the California Medical Association, on an affiliate basis, of undergraduate medical students attending medical schools in this state.

Section 3.—Rights and Privileges of Membership

(a) *Active Members.* Subject to the provisions of the Constitution, all active members shall have the right of suffrage and all other rights and privileges of the Association.

(b) *Associate Members.* Subject to the Constitution, associate members shall have all of the rights and privileges of active members, except the right to vote or hold office.

(c) *Retired Members.* Subject to the Constitution, retired members shall be entitled to receive publications of the Association at such rates as the Council from time to time may determine. Retired members shall not have the right to vote or to hold office. Retired members shall not be required to pay dues unless the House of Delegates determines otherwise, and then the rate of dues shall be fixed by the House of Delegates.

(d) *Honorary Members.* Subject to the Constitution, honorary members shall not be obliged to pay

dues and shall not have the right to vote or to hold office.

(e) *Life Members.* Life members, as a condition to election as such, shall pay to the Association such sum as may be fixed by the Council as a life membership fee. In each year the Council, at its annual organization meeting, shall determine the life membership fee for the ensuing year, basing same on the life expectancy of applicants in various age groups and upon the amount of existing annual dues for active members. In fixing life membership dues the Council may fix different amounts for different age groups. Subject to the foregoing provisions, the fee for life membership in each year shall be uniform and applicable to all active members falling within the respective classifications, as determined by the Council. After payment of the life membership fee, life members shall not be obliged to pay dues and shall not be liable for assessments of any kind or nature. If active membership in good standing is maintained in his component society, each life member shall have the right to vote, to hold office, and shall have all other rights and privileges of the Association. If active membership in his component society is not maintained, the rights and privileges of a life member shall be those of a retired member.

(f) *Affiliate Members.* Affiliate members shall not have the right to vote or hold office, and may be elected to such membership for specified terms and subject to continuance of student, interne or hospital resident status, but shall have all other privileges of membership.

(g) *Additional Classes of Membership.* Subject to the Constitution, the House of Delegates may from time to time establish special and limited classes of membership and fix the dues, qualifications, duration and privileges of such membership.

Section 3.—Termination of Membership

(a) *By Expulsion from Component Societies.* Expulsion from any component society, after due proceedings in accordance with these By-Laws, upon becoming final terminates all the rights and privileges in this Association of the member so expelled.

(b) *By Failure to Pay Dues.* If the annual assessment of dues, payable to this Association by any member of this Association, is not paid on or before April 1 of any year, such member shall automatically lose his membership in this Association as of April 1 of such year. The Council of this Association, in its discretion, upon payment of such unpaid dues, and any other assessments or dues accruing thereafter, may at any time reinstate such member.

(c) *By Revocation of Physician and Surgeon's Certificate.* Any active member whose license to practice medicine and surgery in the State of California is revoked shall, upon receipt of written evidence of such revocation by the Secretary of this Association, thereupon cease to be a member of this association.

(d) *Acts and Conduct Subjecting Member to Censure, Suspension or Expulsion by Component Society.* Any active member of a component society who has been adjudged guilty of a criminal offense involving moral turpitude, or who has been duly adjudged guilty by his society, in accordance with the procedural requirements of these By-Laws, of gross misconduct as a physician or a surgeon or of a violation of any of the provisions of the constitution or by-laws or principles of professional conduct of his society or of the principles of medical ethics promulgated from time to time by this Association or by the American Medical Association, shall be subject to censure, suspension or expulsion from his society by such component society.

(e) *Right of Committee on Membership and Organization of This Association to Prefer Charges.* If a member of this Association is believed by the Committee on Membership and Organization of this Association to be guilty of conduct justifying censure, suspension or expulsion from his component society, said committee may prefer written charges in the form and in the manner hereinafter specified with the secretary of the accused member's county society and may, through a member or members thereof, perform all acts that are reasonably necessary and proper in the prosecution of said charges.

Section 4.—Disciplinary Procedure

(a) *Disciplinary Procedure for Component Societies.* The procedure to be followed by each component society with respect to the censure, suspension or expulsion of a member shall be:

(1) *Charges; Formal Requirements; a Formal Charge Must First Be Made.* Such charge must be in writing, signed by the accuser, and if made by a person other than a member of the society must be sworn to before an officer of the State of California authorized to administer oaths. Charges must state the acts or conduct complained of with reasonable particularity.

(2) *Charges; Filing; Secretary's Duties; Presentation to Board of Directors (or Grievance Committee).* Charges must be filed with the secretary of the accused member's component society. At the first regular or special meeting of the Board of Directors of such component society held after charges are filed, the secretary must present said charges to the Board. The Board of Directors shall then or at any adjournment of said meeting, but not more than thirty days after the date of such regular or special meeting, consider the charges, and in its discretion determine whether or not further proceedings shall be conducted. If the Board determines that no further action shall be taken, the charges shall be dismissed.

If a component society has no board of directors and more than ten members, its members must, at a regular meeting of the society, elect a grievance committee of not less than five (5) active members in good standing; two members shall be designated by the society to serve for a period of one year, two members shall be designated to serve for a period of two years, and one member shall be designated to serve for a period of three years. At the expiration of the terms of office of the respective members of such

committee, successors shall be elected in like manner to serve for a period of three years each. Such grievance committee shall exercise all the power and perform all the duties herein conferred upon boards of directors in the manner and within the times herein provided. If a society has less than eleven members, the entire society, exclusive of the accuser and accused, shall constitute the grievance committee. All references herein to board of directors shall be deemed to include boards of councilors and such grievance committees, and component societies of ten members or less.

(3) *Service of Charge Upon Accused.* If the Board of Directors determines that further action, with respect to said charges, shall be taken, the Board must, within fifteen (15) days after such decision, cause a copy of the charges to be served upon the accused by personally delivering a copy thereof to him, or by depositing a copy thereof in the United States mail, registered and addressed to the accused either at his last known office or at his last known residence.

(4) *Time and Place for Hearing; Service of Notice Thereof.* The Board of Directors shall, at said meeting at which its decision to proceed is made, fix a time and place for a hearing of said charges. Written notice of the time and place set for the hearing shall be served upon the accused within fifteen (15) days by personal delivery or registered mail as aforesaid.

The time so set for a hearing shall be not less than fifteen (15) days after the accused has been served as aforesaid, with a copy of the charges and with the notice of the time and place set for the hearing; said hearing must be held within the county in which the accused holds his county society membership. The hearing before the Board of Directors must actually commence within six months from the date of the filing of written charges. Failure to comply with this requirement shall constitute an automatic dismissal of the charges.

(5) *Right of Accused to Answer; Time to Answer; Formal Requirements.* The accused may, not less than five (5) days before the time set for a hearing, answer said charges. The answer shall be in writing and the original and three copies shall be filed with the secretary of the society; provided, however, that the failure of the accused to answer shall not be deemed to be an admission of the truth of the charges or a waiver of the accused's right to a hearing with respect to said charges.

(6) *Rules Governing Hearing; Duties of Referee of Society; Advice as to Procedure Only.* The Board of Directors shall give ample opportunity both to the accuser and the accused to be heard in person, and to present all testimony, evidence, or proofs which the accuser or the accused may deem necessary, provided that the Board may reject all testimony, evidence, or proofs, which in the judgment of the Board are immaterial, irrelevant or unnecessarily repetitious.

Either the Council or the Executive Committee of the California Medical Association, whenever it shall come to the attention of either thereof that a disciplinary proceeding is pending before any component society, may of its own motion, and shall, upon the request of such component society or of the member or members thereof the subject of any such disciplinary proceeding, appoint a referee who may, but need not be, a member of the California Medical Association, and shall cause the Secretary of the California Medical Association to notify the secretary of such component society of such appointment. The referee so appointed shall preside at the hearing of said charges and shall make all decisions concerning the admission or rejection of testimony or other evidence and procedure. The referee shall not, however, have any voice nor participate in any manner in the determination by the Board of Directors of the disposition of the charges. During the hearing the referee shall perform all duties normally performed by the presiding officer of the Board of Directors.

(7) *Record of Proceedings; Shorthand Reporter; Duty of Secretary to Preserve Board Records; Right of Accused to Copy.* The secretary shall preserve the original of said charges with a certificate of personal delivery or of mailing of a copy or copies thereof, as the case may be, the original notice of the time and place set for the hearing with a certificate of personal delivery or of mailing of a copy or copies thereof, as the case may be, and the original of the answer filed by any member accused if an answer be filed. At the hearing, the Board of Directors shall, at the expense of the society, employ a competent shorthand reporter to record and transcribe into typewriting testimony adduced on behalf of the accuser and the accused and all rulings made. The original charges with certificate of service thereof, the original notice of time and place for hearing with certificate of service thereof, the answer or answers, if any be filed, all documentary evidence introduced at the hearing, the typewritten transcript of the testimony and the written decision of the Board of Directors shall constitute the record of the entire proceedings. The Secretary shall, upon receipt from accused of a sum sufficient to defray the cost thereof, cause a copy or copies of such record to be transcribed, certified and furnished to the accused.

(8) *Decision of Board; When Must Be Written; Rules Governing Vote of Board.* The Board of Directors, after having given the accuser and the accused member full opportunity to be heard, shall conclude the hearing and shall render its decision in writing not more than thirty (30) days thereafter. Hearing shall include any oral arguments and the filing and consideration of any written briefs. The Board of Directors by a two-thirds affirmative vote of all the eligible members of the Board present and voting may exonerate or may censure, suspend or expel the accused member as the facts in its opinion may justify.

The decision of the Board of Directors may be expressed in resolution adopted by said vote. The decision may not contain an opinion and need only be

signed by the secretary or the acting secretary of the component society.

The failure of at least two-thirds of all the members of the Board of Directors present and voting to agree upon the disposition of the charges shall act automatically as a dismissal of the same. No member of the Board of Directors not present at the said hearings for the entire time thereof shall be entitled to vote with respect to the disposition of the charges.

(9) *Suspension; Maximum Period; Status of Suspended Member.* If the Board of Directors shall determine to suspend an accused member, the term of such suspension shall be within the discretion of the Board, provided that in no case shall a member be suspended for a period greater than one year. A suspended member shall have no rights or privileges in the society, provided that at the expiration of the period of suspension such suspended member shall not be reinstated to membership in good standing until he applies for reinstatement and pays all dues accrued during said period of suspension.

(10) *(a) Board's Decision; Secretary to Send Copies.* Within ten (10) days after the decision of the Board of Directors, the secretary of the society shall transmit a copy of the decision to the Board, to the accused member or members and to the Secretary of this Association.

(b) Board's Decision Final; Subject to Appeal. The action of the Board of Directors of a component society shall be final, subject only to appeal to the Council of the California Medical Association in such cases as are provided in these By-Laws.

The decision of the Board of Directors shall not become effective until the expiration of ten days after time during which an appeal may be taken to the Council of this Association. Filing an appeal with the Secretary of this Association shall automatically stay the execution of the decision of the Board of Directors of the component society until written notice of the action of the Council of this Association with respect to appeal has been received by the secretary of the component society from which the appeal was taken.

(c) Technical Rules of Evidence Not to Govern Disciplinary Hearings. All hearings with respect to the disposition of charges against a member of a component society shall be held and conducted in such manner as to ascertain all the facts fairly to the accuser and accused, eliminating all formal or technical rules and requirements which ordinarily pertain to judicial proceedings.

(d) Members Agree That No Cause of Action Shall Accrue. Any person so charged, censured, suspended, or expelled shall have no claim or cause of action against this Association, a component society or any member, director, councilor or officer, thereof by reason of such charges, or the hearing or the consideration thereof or censure, suspension or expulsion therefor.

(e) Expelled Members; Right to Apply for Membership; When Accrues. Any person whose membership has been involuntarily terminated in a component society by reason of violation of these By-Laws may apply for membership after the expiration of one year from the date said membership was terminated, and such application shall be considered in the same manner as a new application for membership.

Section 5.—Procedure for Appeal to Council

A member of a component society censured, suspended or expelled by his county society may appeal from the action of such component society to the Council of this Association within the period of two months succeeding the date of such censure, suspension, or expulsion. Appeals shall be in writing and be filed within the said period of two months in the office of the Secretary of this Association. Said appeal shall be accompanied by a copy of the record of the entire proceedings before the component society duly certified by its secretary, provided the Chairman of the Council may, in his discretion, extend the time of the appellant to file said record. Upon the filing of an appeal the secretary shall present it to the first subsequent meeting of the Executive Committee or the Council. Appeals shall be heard by the Council only after reasonable notice of not less than ten (10) days in writing of the time and place of the hearing of the appeal has been given to the appellant member and the president and secretary of the component society as provided in Section 4 hereof.

Section 6.—Rules Governing Appeals

In hearing appeals, the Council shall review all questions of procedure, and may, in its discretion, review the evidence contained in the record of the original proceedings held before the Board of Directors of the component society. The Council may make findings of fact contrary to, or in addition to, those made by said Board of Directors. Such findings may be based on the evidence adduced before said Board of Directors, either with or without the taking of evidence by the Council. The Council shall use any lawful means which in its judgment will best and most fairly present all the facts involved. The Council may, for the purpose of making such findings or for other purpose in the interest of justice, take additional evidence of or concerning facts material to the questions involved, or may, for such purpose, appoint a committee of its members or any notary public to act as referees or referee for the taking of such additional evidence

Such referee or referees shall render a report in writing to the Council, which report shall contain a clear statement of the facts found by the referee or referees from the testimony or evidence adduced.

The Council may affirm, reverse or modify the decision of the Board of Directors or make such other disposition of the proceedings as it may deem proper.

In every case of an appeal the individual councilors and the Council, through a committee thereof, prior to any hearing being held upon the appeal, shall exert all proper efforts at conciliation and compromise.

This Association may be represented by its attorney to advise the Council upon procedural questions only.

The decision of the Council shall be final and bind the appellant member and the component society.

Section 7.—Registration at Annual Sessions Necessary for Participation Therein

Each member in attendance at the Annual Session shall register, after his right to membership has been verified by reference to the records of this Association. No member shall take part in any of the proceedings of the Annual Session until he has complied with the provisions of this section of the By-Laws.

Section 8.—Component Society Secretaries to Furnish Date on Applications for Membership

The secretary of each component society, on forms or blanks supplied by this Association for that purpose, shall notify the Secretary-Treasurer of this Association in writing, as soon as possible, of each application for membership in such component society, with the name, address, and all other particulars regarding the applicant known to the secretary of such component society.

Section 9.—Component Society Membership

Lists to Be Sent to Secretary-Treasurer. It shall be the duty of the secretary of each component society to furnish the Secretary-Treasurer before the first day of March of each year a list of names and addresses of all members in good standing on the first day of January of each year, and to notify in writing the Secretary-Treasurer of this Association monthly of all changes in membership of the component society, with corresponding changes of address.

Section 10.—Membership Where No Component Society Exists

Any Doctor of Medicine residing in an area in which there is no component society may apply for membership in the component society most convenient to the area in which he practices medicine, and if otherwise qualified he may be elected to membership therein.

Section 11.—Membership Where Major Office and Residence Are in Different Component Society Areas

A Doctor of Medicine may apply for membership only to that component society whose charter covers the area in which his major office for professional practice is located.

Section 12.—Membership as Affected by Transfer of Location of Office

A member who changes his office from the county through whose component county society he holds membership in this Association, to another county in which there is a component society, is eligible to membership in the component society of his new location on the presentation of a transfer card, and satisfactory evidence that his dues have been paid in full in the component society in which he holds membership; provided, however, that no evidence which would disqualify him for membership exists.

He shall forfeit his membership in this Association one year after such change of location of practice unless after proper application he is elected to membership in the society of the county to which he has moved.

Any member who has heretofore changed his location of practice as aforesaid shall have one year after the date of adoption hereof to comply with the provisions of this section.

Section 13.—Transfer Cards

When a member in good standing in a component society moves to another county or other jurisdiction in this State he shall, on request, be given a transfer card, without cost. He must assume such financial obligations as shall be deemed proper by the component society to which he is transferred, and to which he makes application for membership by transfer.

CHAPTER III.—HOUSE OF DELEGATES

Section 1.—Functions of the House of Delegates

(a) In addition to its legislative functions, the House of Delegates shall fix the annual dues to be paid by members, levy assessments, raise funds, act on budgets submitted by the Council and approve any expenditures for special purposes in excess of a contingency fund.

(b) It shall elect the Speaker and Vice-Speaker of the House of Delegates at the regular session. Nominations for these offices shall be made by delegates from the floor.

(c) It shall nominate and elect the President-elect and such other officers as are provided herein or in the By-Laws.

(d) It shall nominate and elect Delegates to the House of Delegates of the American Medical Association in conformity with the Constitution and By-Laws of the latter.

Section 2.—Secretaries of Component Societies to Furnish Lists of Delegates and Alternates

Not later than forty-five days prior to the next scheduled session the Secretary of each component society shall forward to the Secretary-Treasurer of the Association on blanks previously provided, by the Association, the names and addresses of the delegates and alternates elected by the respective component societies and shall certify thereon the dates of election and expiration of terms of service of each delegate and alternate. The Secretary of each component society shall also designate in such list of delegates and alternates the order of priority amongst alternates to be followed by the House of Delegates in seating alternates in lieu of delegates from such component society.

Failure to conform to this provision shall constitute grounds for disqualification of the delegation in default for the scheduled session, at the discretion of the House of Delegates.

Section 3.—Representation

Each component society shall be entitled to one delegate for every one hundred (100) active mem-

bers, or fraction thereof, as of the first day of the preceding November.

Section 4.—Limitations on Seating of Delegates

Only duly elected delegates or alternates may be seated at any session of the House of Delegates unless the Secretary of the Association has been given due notice of substitution at least fifteen (15) days in advance of the session.

Section 5.—Disqualification of Delegates or Alternates for Absence From a Session

Any delegate absent without good cause from two or more consecutive meetings of the House of Delegates, and who has failed to give fifteen days' notice to the Secretary of the Association of his inability to be present, shall thereupon be disqualified as a delegate and, in addition, ineligible for re-election as a delegate or alternate for three years immediately succeeding the expiration of his term; except that the Committee on Credentials may excuse absence on presentation of good cause therefor. If the component society has not designated the alternate to replace an absent delegate, the Committee on Credentials may determine the order of seating alternates from such component society.

Section 6.—Notification of Delegates

The Secretary of each component society promptly shall notify in writing each delegate and alternate immediately after his election to such office, and shall expressly direct each delegate's and alternate's attention to the provisions of Section 5 above.

Section 7.—Qualifications of Delegates and Alternates

(a) At least three (3) years' active membership in good standing in the component society immediately preceding election shall be required for election as delegate or alternate.

(b) Only duly elected delegates, or properly qualified alternates, may be seated with the right to vote.

(c) Officers of the Association who by virtue of their offices shall be delegates may be seated but shall have no right to vote.

Section 8.—Sessions and Meetings

(a) In each year there shall be one regular session of the House of Delegates; the time and place of such regular session to be determined by the Council as far as possible in advance and notice thereof published in the Journal of the Association. There shall be at least two meetings of the House of Delegates at each regular session, with one day intervening between the first and second meetings; at its second meeting the House of Delegates may decide upon a third meeting of such session and elect to recess to any place in California and time (not more than six months later) desired.

(b) In addition to regular sessions, special meetings of the House of Delegates may be called at any regular or special meeting of the Council, by a two-thirds vote of all the members of the Council, or by written call stating the object of the meeting, filed with the Secretary in the office of the Association and signed by one-half or more of the members of the House of Delegates. Upon the filing of such call with the Secretary, the Council shall within thirty (30) days thereafter fix the time and place for the holding of such special meeting and cause written notice thereof stating the object of the meeting to be sent by United States mail, postage fully prepaid, to each member of the House of Delegates, addressed to him at his office or place of residence, as shown by the records of the Secretary's office, at least fifteen (15) days prior to the date of meeting.

(c) Officers of the Association shall be elected at the regular session.

(d) It is the policy of the Association that all resolutions shall be submitted to the secretary at least 30 days in advance of each regular session and be published to the delegates as soon as possible; however, all resolutions presented before or during any session shall be referred to the proper Committee on Resolutions for consideration and recommendation.

(e) Action on resolutions may be taken at the second or third meeting of any session. The House of Delegates may refer to the proper committee for further study any resolution, in which event the committee shall make available to each delegate and alternate copies of said resolution and the recommendations of the committee, through the office of the Association, at least thirty (30) days in advance of the date of the next meeting at which action on said resolution is to be taken.

Section 9.—Budget

The House of Delegates shall act on an annual budget submitted to it by the Council and shall approve such budget either as submitted or revised by the Council or the House of Delegates.

Section 10.—Division of Scientific Work

The House of Delegates, either upon recommendation of the Council or on its own initiative, shall provide for division of the scientific work of the Association among appropriate sections and assemblies.

Section 11.—House of Delegates Committee

Prior to or at the commencement of each regular session the Speaker of the House shall appoint from the members thereof the following committees:

1. A Committee on Credentials,
2. A Reference Committee on Finance,
3. A Reference Committee on the reports of Officers, Council, Standing and Special Committees, and
4. Two or more Reference Committees on resolutions, amendments to the Constitution and By-Laws, and new and miscellaneous business (the Speaker may allocate amongst these committees all business properly referable to them).

Section 12.—Membership of Credentials and Reference Committee

Each of the aforesaid committees shall consist of three members, the chairman of each to be designated by the Speaker.

The Speaker, the House concurring, shall refer said reports, resolutions, and business to the respective Reference Committees, but may allocate among them any of said reports, resolutions or portions thereof, and other business, to avoid duplication and to expedite the business of the House of Delegates.

Each Reference Committee shall prepare a written report dealing with and making recommendations on all matters submitted to it. In those instances in which resolutions or other matters remain before a Reference Committee between meetings of the House of Delegates, copies of such resolutions or other matters and the recommendations of the committee thereon shall be mailed or delivered by the Secretary to each elected Delegate and Alternate at least thirty days (or if less than thirty days intervenes between meetings, as early as possible) prior to the meeting of the House of Delegates at which such resolutions or other matters and recommendations concerning them are to be considered. The report of each committee may be acted upon as a whole or section by section, as the House may determine.

Section 13.—Special Committees of House of Delegates

The Speaker, the House of Delegates concurring, shall have the right to appoint special committees for special work. All committees of the House of Delegates shall present their reports to the House of Delegates in writing.

Section 14.—Duties of Credentials Committee

The Secretary of the Association shall supply the Committee on Credentials with the necessary information concerning the membership of the House of Delegates.

The Secretary shall give this committee a list of component societies, showing the total membership as of November 1 of the preceding year. This committee shall ask each delegate and alternate to present his written credentials, but shall accept the official written list submitted by the secretary of any component society; provided that such written list be sent to the Secretary of the Association at least fifteen days before the beginning of the annual session.

The Committee shall make a written report to the House of Delegates of the delegates and alternates entitled to membership therein.

Section 15.—Delegates to the American Medical Association

The House of Delegates shall elect delegates and alternates to the House of Delegates of the American Medical Association in accordance with the Constitution and By-Laws of that organization.

Section 16.—Special Committees Appointed by House of Delegates

The House of Delegates shall have authority to appoint committees for special purposes from among members of the Association who may or may not be members of the House of Delegates. Such committees shall report in writing to the House of Delegates; and the members, the House concurring, may participate in the debate on their reports.

Section 17.—Approval of Memorials

The House of Delegates shall approve all memorials and resolutions issued in the name of the Association during an annual session before they shall become effective.

CHAPTER IV.—COUNCIL

Section 1.—Auditing Committee of Council

The Chairman of the Council, subject to its approval, shall appoint an auditing committee of three members, designating one of the members as its chairman.

The Auditing Committee shall inspect all bills and claims against the Association, and no bill or claim shall be paid except upon voucher or draft having the approval of at least two of the three members of the Auditing Committee; provided, however, that any bill or claim may be paid without the approval of any member of the Auditing Committee by a majority vote or written approval of a majority of all the members of the Executive Committee.

Section 2.—Executive Committee of Council

The Executive Committee shall consist of the President, President-Elect, Chairman of the Council, Chairman of the Auditing Committee, and one other member of the Council (elected by the Council at its organization meeting each year). The Secretary-Treasurer and Editor shall be members ex officio, but without the right to vote. The organization, duties and powers of the Executive Committee shall be as provided in the By-Laws.

Section 3.—Council: Organization

At the first meeting of the Council held after the adjournment of the last meeting of the House of Delegates at the regular annual session of the Association, the Council shall organize by the election of one of the Councilors as Chairman of the Council, who shall serve as such up to the first Council meeting held after the adjournment of the last meeting of the House of Delegates of the next succeeding regular annual session of the Association; and a Vice-Chairman who shall hold office for the same term, and who, in the absence of the Chairman, shall perform the duties of the Chairman. The Secretary-Treasurer of the Association shall serve as the secretary of the Council.

Section 4.—Duties of District Councilors

Each District Councilor shall be organizer, peacemaker and censor for his district.

(a) *Visitation of Component Societies; and Report Thereon.* He shall visit each county in his district at least once a year for the purpose of organizing component societies where none exist, of inquiring into the condition of the profession, and of maintaining touch with the activities of the component societies of his district. He shall in writing make an annual report of this work and of the condition of the profession of each county in his district to the Coun-

cil, which shall take such action thereon as it may deem best.

(b) *Expenses of Councilors and Officers.* Councilors and officers shall be allowed railroad fare or mileage not exceeding 5 cents a mile, plus an allowance for maintenance expense of ten dollars a day, while absent from their places of residence; (a) in attending association, district or county society meetings; (b) meetings of committees of the Association; (c) authorized councilor or officer visits to county societies; (d) and otherwise when on official business, authorized or approved by the Council.

Section 5.—Mail Ballot

The Chairman of the Council, at any time, may direct the Secretary to submit any urgent matter or question to the members of the Council by mail ballot, the question or proposition being prepared through conference of the Secretary with the Chairman of the Council and the Chairman of the Executive Committee; and the vote of two-thirds of the members upon such question by mail or telegraph shall be binding upon the Council.

Section 6.—Registry

The Secretary-Treasurer, in writing, shall request each Councilor to register his address where he desires all notices to be sent to him by mail or telegram.

Section 7.—Order of Business

At meetings of the Council, business shall be transacted as the Council may determine from time to time by resolution.

The Council shall provide and fix the order of business of the first two meetings of the House of Delegates at each regular annual session, provided that the House of Delegates may change the order of business by a majority vote.

Section 8.—Preparation of Budget; Annual Assessment

The Auditing Committee, prior to December 1 of any year, shall submit to the Executive Committee, for consideration at its December meeting, a budget under which the Association shall work in the fiscal year following the next annual session.

The Executive Committee, after consideration of the Auditing Committee's proposed budget, shall submit the same to the Council, prior to the spring meeting of the Council, with a report of its own containing suggested changes, additions, or comments.

The Council in turn shall consider the two proposed budgets so submitted, and shall then make a final draft of a proposed budget for the Association, to be submitted to the House of Delegates at the next annual session.

The Council shall recommend to the House of Delegates the amount of the annual dues or assessments of each member of the Association.

Section 9.—Committee on Arrangements for Annual Meeting

(a) *Appointment and Duties.* The Chairman of the Council, subject to the approval of the Council, shall, at least six months before the regular annual session, appoint a Committee on Arrangements for the annual session, one member thereof being designated as the general chairman. This committee shall consist of five members, at least three of whom shall be members of the component society of the county in which the annual session is to be held.

The Secretary-Treasurer of the Association shall be ex officio a member of this committee.

This committee shall have charge of all local arrangements not otherwise provided for.

The terms of office of members of this committee shall expire when the succeeding committee on arrangements is appointed.

As the local Committee on Arrangements this committee shall provide suitable meeting places and shall have general charge of all local arrangements. The committee shall have power to appoint local advisory members and subcommittees to aid in its work.

(b) *Commercial Exhibit.* The Council shall decide what portion of the income from commercial exhibits or other convention services shall go to the local Committee on Arrangements. The location and rules for the commercial exhibits and other accessory annual session activities shall be subject to the approval of the Council.

(c) *Local Convention Expenses.* The Council shall decide what portion of the local expenses shall be borne by the Association.

(d) *Report on Committee on Arrangements.* The Committee on Arrangements shall, as soon as possible and not later than two months after the adjournment of the final meeting of the regular annual session, make and file with the Secretary-Treasurer of the Association an itemized, detailed report of all of its receipts and disbursements, and shall remit any moneys due the Association remaining in its possession, to the Secretary-Treasurer.

Section 10.—Offices

The Council shall provide and secure such offices for the Association as may be required to conduct its activities and business properly.

Section 11.—Executive or Field Secretaries or Representatives

The Council may employ one or more Executive or Field Secretaries or Representatives, who need not be physicians nor members of the Association. The duties of such a representative or representatives, if appointed, shall be determined by the Council by resolution.

Section 12.—Legal Counsel

The Council at its annual organization meeting shall appoint one or more legal advisors, giving each such title as may be deemed proper. It shall fix the amount of retainer and other fees. By resolution it shall indicate what duties shall be assigned to each advisor. The Council shall appoint such attorneys-at-law licensed in California at its annual organization meeting.

The Council shall have the right to request the attendance of Counsel of the Association at any meetings at which it might desire his presence and advice, and at such meetings he shall call the attention of the Council to matters in which the legal aspects may be of importance, and shall give such other opinions in special matters as may be requested of him by the Council.

The General Counsel shall present in writing as promptly as the same may be properly prepared, such legal opinions as may be requested by the House of Delegates, the Council or the Executive Committee.

CHAPTER V.—COMMITTEES

Section 1.—Standing Committees

The standing committees of this Association shall be as follows:

(a) Scientific Work
(b) Public Policy and Legislation
(c) Medical Defense
(d) Medical Education and Medical Institutions
(e) Hospitals, Dispensaries, and Clinics
(f) Medical Economics
(g) Associated Societies and Technical Groups
(h) History and Obituaries
(i) Industrial Practice
(j) Postgraduate Activities
(k) Public Relations
(l) The Reference Committees of the House of Delegates

until final adjournment of each regular session.

Section 2.—Standing Committees; How Elected; Term of Office

Unless otherwise provided in these By-Laws, each of the standing committees (except House of Delegates Reference Committees) shall consist of one member of the Council and two other members. Members of standing committees (other than House of Delegates Reference Committees) shall serve for a term of three (3) years. One member of each of these committees shall be nominated annually by the Council and if approved by the House of Delegates shall be deemed elected.

Section 3.—Report Procedure for All Committees

Regular standing and special committees of the Association may make investigations and surveys on authorization of the Council or House of Delegates, but all recommendations and reports of all committees (unless expressly otherwise provided in the Constitution or By-Laws) must be submitted only to the Council or House of Delegates. Other than as herein stated no committee is authorized to act for or represent this Association.

Section 4.—Advisory Groups to Standing Committees

To aid it in its work, each committee, if it so desires, shall have the power to appoint an Advisory Group to its committee, consisting of from two to ten members. Such advisory members, if present at a regular committee meeting, shall not have the right to vote.

Section 5.—Officers of Standing Committees

The chairman of each of these committees, except the Committee on Public Relations, shall be nominated and elected annually by the Council, by and with the approval of the House of Delegates. The chairman of the Committee on Public Relations shall be elected by said committee, subject to the approval and confirmation of the Council, and in the event of a failure to elect within sixty days after adjournment of the annual session the Council shall elect said chairman. Each of these committees shall, each year, except as otherwise provided in these By-Laws, at its first meeting or official consultation, during or following the annual session elect its own secretary.

Section 6.—Secretary-Treasurer's Notice to Standing Committees

The Secretary-Treasurer of the Association, within one month after the annual session, shall write the Committee Chairman of the preceding year, to call a meeting for organization and consideration of any business. The Secretary shall also send a copy of this letter to each of the other members of the committee.

Section 7.—Annual Reports of Standing Committees

At least sixty days prior to the annual session, each of these committees shall submit a written report to the Council on its work during the preceding year, the same to be printed in the Pre-Convention Bulletin as otherwise provided.

Section 8.—Committee on Scientific Work

The Committee on Scientific Work shall consist of the Secretary-Treasurer, the secretaries of the sections on general surgery and general medicine and three other members to be elected by the Council, each of these three members to serve three years, one member being elected each year. The Secretary-Treasurer shall be chairman.

This committee shall determine the character and scope of the scientific proceedings of the Association for each session, and shall invite the guest speakers, subject to the instructions of the Council.

At least thirty days previous to each annual session it shall prepare and issue a program announcing the order in which papers and discussions shall be presented.

This committee shall have one joint session with the section secretaries, at a time and place to be designated by the chairman of the committee, at least forty-five days prior to the annual session, to coordinate more efficiently the various activities of the Association at its annual session. The chairman of the local committee on arrangements shall be invited to attend this meeting.

Section 9.—Committee on Public Policy and Legislation

The Committee on Public Policy and Legislation shall consist of three elected members, and ex officio, the President and President-Elect.

The chairman of the committee, and in his absence, the President, shall act as chairman at the joint

meetings of this central state group and of auxiliary county groups.

(a) *Functions of the Committee.* The Committee on Public Policy and Legislation and its auxiliary county groups shall represent the Association in securing and enforcing legislation in the interest of public health and of scientific medicine, subject, however, to the approval of the Council.

(b) *County Auxiliary Committees on Public Policy and Legislation.* Each component society shall appoint or elect three of its members as members of its auxiliary Committee on Public Policy and Legislation, designating one member as chairman; and the component society secretary shall send promptly the names and addresses to the Secretary of this Association.

(c) *Work of Auxiliary County Committees.* The Committee on Public Policy and Legislation of this Association, with the sanction of the Council, shall formulate the duties of these county auxiliary committees and supply each member with a copy of its suggestions and instructions. The auxiliary committeemen shall be accountable to their component societies and to the Council of this Association for prompt and continued cooperation with the Committee on Public Policy and Legislation of this Association.

Section 10.—Committee on Medical Defense

The Committee on Medical Defense, subject to the approval of the Council, shall prepare plans and establish rules for the protection of the legal rights of members of this Association against whom suits for alleged negligence have been threatened or brought.

It may assist in the defense of any member sued for alleged negligence if the member was in good standing and had complied with the rules of the Council when the service on account of which suit was threatened or brought was rendered—provided that the committee determines that the position of the member merits such action.

Section 11.—Committee on Medical Education and Medical Institutions

The Committee on Medical Education and Medical Institutions shall serve in this State for the Council on Medical Education of the American Medical Association.

It shall keep in touch with the problems pertaining to medical education and to medical and other institutions of training for medicine and the healing art.

Section 12.—Committee on Hospitals, Dispensaries and Clinics

The Committee on Hospitals, Dispensaries and Clinics shall serve in this State for the Council on Hospitals of the American Medical Association.

It shall keep in touch with the problems arising in the fields of work of all types of hospitals, dispensaries and clinics giving special attention to those activities that are, or tend to become, a menace to the best interests of scientific medicine and of the profession and its members.

Section 13.—Committee on Medical Economics

The Committee on Medical Economics shall investigate matters affecting the economic status of doctors of medicine.

Section 14.—Committee on Associated Societies and Technical Groups

The Committee on Associated Societies and Technical Groups, subject to the instructions of the Council, shall endeavor to create proper liaisons between this Association and other state and national medical organizations, as well as with the organizations of related professions, such as dentistry, pharmacy and nursing. It shall also endeavor to bring about a proper understanding with non-medical organizations or groups of technicians and others whose work has a bearing on or is related to the practice of medicine.

Section 15.—Committee on History and Obituaries

The Committee on History and Obituaries shall compile and prepare for the archives and for the publications of the society suitable articles on the history of the Association and statements concerning deceased members. The Editor and the Secretary shall be members of this committee, ex officio.

Section 16.—Committee on Industrial Practice

The Committee on Industrial Practice shall keep in touch with matters and problems peculiarly connected with industrial practice.

Section 17.—Committee on Postgraduate Activities

The Committee on Postgraduate Activities, of which the Secretary-Treasurer shall be an ex officio member, shall use its best efforts to promote the postgraduate and clinical courses and instruction among the component county units of the Association.

The supervision of such postgraduate and clinical courses and instruction shall be carried on through the central offices of the Association, the Council being empowered to defray travel expenses of guest speakers and other costs incident to such work to such amount as in the judgment of the Council may be deemed proper. In the development of such postgraduate and clinical courses and instruction, it is stipulated that the component societies, through their constituted representatives, shall cooperate with the Standing Committee on Postgraduate Activities and shall also arrange to bear a proper proportion of the expense thereof of such amount as may be mutually agreed upon.

Section 18.—Committee on Public Relations

The Committee on Public Relations shall consist of the chairmen of the following committees: Public Policy and Legislation, Medical Economics, Associated Societies and Technical Groups, and the President and President-Elect.

The committee shall be responsible to the Council and the House of Delegates for all of its activities.

The Council or the Executive Committee may instruct the Committee on Public Relations, and outline to it certain policies and duties which shall be executed through the Director of Public Relations. In the event of any disagreement between the committee and the Council or the Executive Committee as to any activity or policy, the decision of the Council, after full discussion and hearing, shall be final.

The committee shall make recommendations to the Council for approval as to the time, the place, the number of meetings and the budget of the Department of Public Relations, provided that the Secretary shall call the first meeting of the committee within thirty (30) days following the annual meeting of the Association.

The Director of Public Relations shall be appointed by the Council (after consultation with the Committee on Public Relations) annually at the organization meeting of the Council. He shall serve at the pleasure of the Council and the Committee. He shall act under the supervision and instruction of the chairman of the committee in such matters as shall be approved and sanctioned by the committee, and be responsible to the committee.

The Council shall arrange with the general counsel to give the committee all legal aid.

The committee shall annually at its first meeting elect its own chairman, subject to the approval and confirmation of the Council. The Secretary of the Association shall be ex officio secretary. A majority of the committee shall constitute a quorum.

Section 19.—Department of Public Relations

The Department of Public Relations shall consist of the following component standing and special committees of the Association, viz: The Committee on Public Policy and Legislation; the Committee on Medical Economics; the Committee on Hospitals, Dispensaries and Clinics; the Committee on Health and Public Instruction; the Committee on Membership and Organization; the Committee on Industrial Practice; the Committee on Postgraduate Activities; the Committee on Medical Defense and the Cancer Commission.

Section 20.—Publication of Committee Reports in Pre-Convention Bulletin

Reports of the standing and special committees, as approved, deleted or modified by the Council, shall be published in a pre-convention bulletin or in the official journal of the month preceding the date of the annual session of the Association. Such reports must be in the hands of the Secretary-Treasurer at least sixty days in advance of the annual session.

If a committee fails to send in its report in proper time, the name of the committee and the names of its members shall be printed as above indicated, with a statement that the committee failed to send in its report, and the Council, subject to the approval of the House of Delegates, shall be empowered under such conditions to make such changes in the personnel of the committee as in its judgment may be deemed best.

Section 21.—Additional Committees

The House of Delegates and the Council are authorized and empowered to appoint special committees, with special instructions as to work to be undertaken, whenever it is deemed impractical or improper for the contemplated duties to be performed by a standing committee.

Section 22.—Physicians' Benevolence Committee

The Physicians' Benevolence Committee shall consist of three (3) members whose appointments and terms of office shall be as provided in Section 2 of this Chapter.

The Committee shall be responsible to the Council and the House of Delegates for all of its activities.

The committee shall administer those funds, of this Association, hereinafter designated as comprising the Physicians' Benevolence Fund.

The committee's administration of said fund shall be subject to the provisions of this section.

(a) The funds which may from time to time be allocated to it, from the general funds of the Association, by the Council, are the funds for this committee.

(b) All bequests, voluntary contributions, and donations, from any source whatever, that may be received by this Association for the express and implied purpose of aiding needy members, and

(c) All other funds from whatever source derived, except Accounts Receivable, payments for indebtedness to this Association, Dues and Assessments received by this Association, which the payer, donor, or other person transferring the funds, expresses the intent that such funds shall be for aid to needy members.

Funds contained in the Physicians' Benevolence Fund may from time to time be disbursed by the Physicians' Benevolence Committee.

CHAPTER VI.—POWERS AND DUTIES OF OFFICERS

Section 1.—Duties of the President

The President shall preside at all meetings of the Association.

He shall appoint all committees not otherwise provided for; he shall deliver an address at the annual session at such time as may be arranged, and shall perform such other duties as custom and parliamentary usage may require, or as the House of Delegates or the Council may direct.

He shall be the real head of the profession of the State during his term of office, and, as far as practicable, shall visit, by appointment, the various sections of the State and assist the Councilors in building up the component societies, and in making their work more practical and useful. The Council shall decide what portion of the expenses incurred on his official visits shall be paid by the Association.

He shall be ex officio a member of all committees of the Association.

Section 2.—Vacancy in Offices of President and President-Elect; How Filled

In case of vacancy in the offices of both President and President-Elect, the chairman of the Council shall act as the Acting President until a President is elected at the next annual session of the House of Delegates.

Section 3.—Duties of the Secretary-Treasurer, Executive Secretary and Field Representatives

The duties of the Executive Secretary and Field Representatives may be such as are delegated to them by the Council of the California Medical Association, and may be any and all duties as are specified under the various provisions of this section.

(a) *Minutes.* The Secretary-Treasurer (who may also be referred to as Secretary or Treasurer) shall attend the General Meetings of the Association, the meetings of the House of Delegates, of the Council and of the Executive Committee, and shall keep minutes of their respective proceedings in separate record books.

(b) *Custodian of Records.* He shall be custodian of all record books and papers belonging to the Association. He shall have the custody of the seal of the Association.

(c) *Contracts.* He shall countersign all contracts, agreements, conveyances, transfers or other instruments to which the Association is a party, the execution of which has been authorized by the House of Delegates or Council.

(d) *Checks.* The Secretary-Treasurer shall sign and issue checks or drafts only upon vouchers approved and signed by at least two of the members of the Auditing Committee or as otherwise provided.

(e) *Advertisements in Association Publications.* The Secretary-Treasurer, subject to instructions by the Council, shall carefully examine, approve, modify or reject all material for advertising in any of the publications of the Association, and shall, in all cases of doubt, refer such proposed advertisements to the Executive Committee or the Council for decision. He shall, with the approval of the Council or the Executive Committee, execute, for the Association, written contracts relating to advertising in the form approved by the Council, subject to instructions by the Council.

(f) *Registrar at Annual Sessions.* He shall provide for the registration of the members and delegates at the Annual Session.

(g) *Index Register of California Medical Licentiates.* He shall, with the cooperation of the secretaries of the component societies, keep a card-index register of all the licensed practitioners of the State by counties, noting the status of each in relation to his component society; and shall transmit a copy of this list to the American Medical Association, transmitting to its secretary each month a report containing the names of new members and the names of those dropped from the membership roster during the preceding month.

(h) *Register of Component Societies, Their Members and Officers.* He shall keep a register of all component societies, their respective officers, and of all members of the Association, with their addresses, and shall compile an annual directory of the same. He shall print in the January or February issue of the official journal the number of active members of each component society as of November 1st of the preceding year.

(i) *Notices.* He shall give all notices required by the Constitution and By-Laws of this Association, or by order of the Council, or of the Executive Committee, or by law.

(j) *Correspondence and Notifications to Committees.* He shall conduct the official correspondence, promptly notifying members of meetings, officers of their election, and committees of their appointment and duties, as outlined in the motions creating such committees. Such notifications shall be made in writing.

(k) *Assistants.* He shall employ and dispense with such assistants as may be ordered by the Council. The Council by resolution may outline the scope and duties of special employees acting under the Secretary-Treasurer.

(l) *Annual and Other Report Forms.* He shall supply all component societies with the necessary forms for making their annual and other reports to this Association.

(m) *Salary.* The amount of his salary shall be fixed by the Council.

(n) *Bond.* He shall give bond in such sum as may be fixed by the Council. The Association shall pay the premium on the said bond.

(o) *Duties as Treasurer.* He shall as Treasurer demand and receive all funds due the Association, together with bequests and donations, and shall promptly deposit the same in one of the depositaries thereof; and shall keep a proper and accurate record thereof, as well as of all funds disbursed by the Association.

(p) *Audits and Reports.* He shall subject his accounts to such examination or audit as the House of Delegates or Council may order.

He shall annually render an account of his work, and of the state of the funds in his hands, and make a report on the same and of his work as Secretary-Treasurer to the House of Delegates. He shall in writing also make such other reports as the House of Delegates or Council may request.

(q) *Disbursement of Association Moneys.* He shall pay out the money of the Association only upon a check or draft as otherwise provided herein.

(r) *Other Duties.* He shall perform such other duties as the Council or Executive Committee may direct.

Section 4.—Duties and Powers of the Chairman of the Council

The Chairman of the Council shall preside at all meetings of the Council. He shall sign all contracts and agreements, conveyances, transfers or other instruments (other than advertising contracts) to which the Association is a party, the execution of

which has been authorized by the House of Delegates or the Council. He shall sign all checks or drafts for the disbursement of funds of the Association. He shall, on behalf of the Council, deliver its annual report to the House of Delegates. He shall perform such other duties as may be imposed upon him by the Constitution or these By-Laws.

Section 5.—Duties of Vice-Chairman of the Council

The Vice-Chairman of the Council, in the absence or inability of the Chairman to act, shall be vested with all the powers and shall perform all the duties of the Chairman.

Section 6.—Duties and Powers of the Speaker

The Speaker of the House of Delegates shall preside at its meetings and shall perform such other duties as parliamentary usage may require. He shall appoint all committees authorized by the House of Delegates, unless otherwise provided. He shall be ex officio a member of the Council.

Section 7.—Duties of Vice-Speaker

The Vice-Speaker shall act as Speaker in the absence of or at the request of the Speaker.

Section 8.—Duties of the Editor

The Editor and Associate Editor or Editors shall compile, edit and have charge of the official journal of the Association and such other publications as the Council or the House of Delegates may instruct him to undertake.

CHAPTER VII.—SESSIONS AND MEETINGS

Section 1.—Addresses at Annual Session

At the General Meetings, at such times as may have been arranged, shall be delivered the annual address of the President and, with the sanction of the Council, such other addresses and reports as may be deemed desirable.

Section 2.—Time Length of Papers

No address or paper, except that of the President, and such other addresses and reports as may be deemed desirable by the Council, shall occupy more than twenty minutes in delivery.

Section 3.—Time Length of Discussions

No member, except by unanimous consent, shall speak more than once in the discussion of any paper nor longer than five minutes at any one time.

This by-law shall be printed on all programs of general and section meetings.

Section 4.—Scientific Papers Property of Association

All papers read before this Association shall be its property.

Each paper, when it has been read, shall be deposited with the secretary of the section, by him to be promptly turned over to the Secretary of the Association.

Section 5.—Scientific Papers Not to Be Published Elsewhere

Authors of papers read before this Association shall not cause them to be published elsewhere except with the consent of the Committee on Publications.

Section 6.—All Meetings of Same Session Shall Be in Same Locality

The general meetings of the Association, the meetings of the House of Delegates, and the meetings of the Scientific Assembly and its sections at any session shall be held in the State of California at the same locality and in buildings as convenient of access, one to the other, as may be possible.

CHAPTER VIII.—ELECTION OF OFFICERS: TERMS

Section 1.—President-Elect—When and How Elected: Term of Office

The House of Delegates at the regular annual session thereof shall elect the President-Elect to serve until the adjournment of the final meeting of the House of Delegates at its next regular annual session. At the conclusion of the final meeting of the House of Delegates at its next regular annual session, such President-Elect shall assume the office of President, and serve as such for the term of one year thereafter, or until his successor assumes office.

Section 2.—Speaker and Vice-Speaker of House—When Elected: Term of Office

The House of Delegates shall at the regular annual session thereof elect a Speaker of the House of Delegates and a Vice-Speaker of the House of Delegates, each to serve for the term of one year, or until their successors are elected and assume office. The Speaker and Vice-Speaker shall be members of the House of Delegates at the time of their election.

Section 3.—Councilors to Be Elected in Different Years

Five Councilors shall be elected each year.

Section 4.—Council Appointments to Fill Vacancies in Office

The Council by appointment shall fill any vacancy in office not otherwise provided for in this Constitution or the By-Laws, which occurs during the interval between the annual sessions of the House of Delegates. Such appointee shall serve until the next annual session or until his successor has been elected and has assumed office.

Section 5.—Officers Elected by House of Delegates

Those officers who under the Constitution are elected by the House of Delegates shall be elected at the second meeting of the House at the regular annual session thereof.

Section 6.—Election of District Councilors

At least twenty-four hours prior to the second meeting at each regular session of the House of Delegates the delegates from those districts in which Councilor vacancies are about to occur shall sepa-

rately meet, and in each district the delegates shall elect a chairman and a secretary. At such caucus the delegates in each district shall by nomination, secret ballot and majority vote of the delegates present elect a district Councilor from such district to serve for the ensuing term. The chairman of the district delegation shall then report at the second meeting of the House of Delegates the results of the election, and when such report is made the member elected shall thereupon assume office as a district Councilor. The time and place of the caucus of each district delegation shall, in the absence of unanimous written consent by the delegates from the district fixing time and place, be fixed by the Speaker and announced at the first meeting of the House of Delegates at each regular session. In the event that at any district caucus no person receives a majority vote for district Councilor, the chairman of the caucus shall report such fact at the second meeting of the House of Delegates and shall also report the names of all nominees submitted to the caucus, whereupon the House of Delegates shall proceed to elect from such nominees the district Councilor from such district.

Section 7.—Election of Chairman and Vice-Chairman of Council; Employment of Secretary-Treasurer, Assistant Secretaries, Editor and Associate Editors

The Council, at the organization meeting thereof, shall elect a Chairman and a Vice-Chairman, each to serve for the term of one year. It shall also employ a Secretary-Treasurer and an Editor, and, in its discretion, one or more Assistant Secretaries or Associate Editors. The terms of their employment shall be such as are satisfactory to the Council, provided, however, that no contract of employment shall, by its terms, exceed a period of three (3) years from the date of the organization meeting at which such contract is authorized.

Section 8.—Qualifications of Secretary-Treasurer and Editor

No person shall be eligible to the office of Secretary-Treasurer or Editor or Associate Editor who does not hold the degree of Doctor of Medicine, but membership in this Association shall not be a necessary qualification for the offices of Secretary-Treasurer, Editor or Associate Editor.

Section 9.—Election by Ballot; Number of Votes Necessary

All elections of officers shall be by ballot; provided, that by a two-thirds vote of the members present and acting election by ballot may be waived.

A majority of the votes cast shall be necessary to elect any officer, except delegates and alternates to the American Medical Association.

In case no nominee receives a majority of the votes on the first ballot, the nominee receiving the lowest number of votes shall be dropped and a new ballot taken. This procedure shall be continued until one of the nominees receives a majority of all the votes cast, when he shall be declared elected.

Section 10.—Election of Delegates and Alternates to A.M.A.

In case no nominee for delegate or alternate to the House of Delegates of the American Medical Association receives a majority of the votes cast on the first ballot, the nominee receiving the highest number of votes cast shall be declared elected. In case of a tie vote, the tie shall be determined by lot. A separate election shall be held to fill each vacancy, and an alternate shall be specifically elected for each delegate.

Section 11.—When Terms of Office of Speaker, Vice-Speaker and Councilors Begin

The terms of office of the Speaker and Vice-Speaker of the House of Delegates (which terms are herein generally stated to be one year) and the terms of office of the Councilors (which terms are herein generally stated to be three years) shall commence immediately upon the adjournment of the last meeting of the House of Delegates of the regular annual session of the Association at which such officers are elected, and shall continue up to the adjournment of the last meeting of the House of Delegates at the annual session of the Association of the year in which the term of office ends.

Section 12.—Officers to Hold Office Until Successors Are Elected and Assume Office

Every officer shall hold office until his successor has been elected and has assumed office either in person or by announcement.

CHAPTER IX.—SCIENTIFIC SECTIONS

Section 1.

(a) *Division of Scientific Work.* The scientific work of the Association shall be divided into scientific sections, as follows: General Medicine; General Surgery; Pediatrics; Eye, Ear, Nose and Throat; Urology; Anesthesiology; Obstetrics and Gynecology; Radiology; Industrial Medicine and Surgery; Pathology and Bacteriology; Dermatology and Syphilology; Neuropsychiatry; General Practice; Public Health; and Allergy.

(b) *Additional Scientific Sections; How Authorized.* Additional scientific sections or regrouping of existing scientific sections can through proper resolution be authorized by the House of Delegates.

(c) *Rules of Procedure of Scientific Sections.* Each scientific section shall adopt rules of procedure for its own better government and work. Its officers shall be responsible for the proper keeping of records of scientific and business meetings.

(d) *Officers of Sections.* The members of each section shall at the regular annual session of the Association elect a chairman and a secretary to serve for the term of one year.

(e) *Program.* Each of the sections shall present a scientific program at the annual session of the Association, and its officers shall be responsible for the proper preparation of the same, and for the proper cooperation with other scientific sections during the annual meeting.

CHAPTER X.—FUNDS, PROPERTY AND ASSESSMENTS

Section 1.—Reduction of Dues

The House of Delegates may reduce annual dues of active members, as follows:

(a) Those active members who have been in the practice of medicine for less than one year (on the first day of the calendar year for which such dues are payable), may be reduced to one-fourth regular dues;

(b) Those active members who have been in the practice of medicine for less than two years (on the first day of the calendar year for which such dues are payable), may be reduced to one-half regular dues;

(c) Those active members who have been in the practice of medicine for less than three years (on the first day of the calendar year for which such dues are payable), may be reduced to three-fourths regular dues.

Dues payable by associate members shall be uniform and equal but may be set at not less than one-half the regular dues for active members.

Section 2.—Annual Dues and Assessments

(a) *When Payable.* The annual assessment or dues shall be payable on or before January 1 of the year for which they are levied.

(b) *County Secretaries to Collect Dues.* The secretary of each component society shall cause to be collected and shall forward to the office of the Association the dues and assessments for its members.

(c) *Record of Fact of Payment of Dues.* The record of payment of dues and assessments on file in the office of the Association shall be final as to the fact of payment by a member and as to his right to participate in the business and proceedings of the Association and of the House of Delegates.

(d) *Dues of New Members; Amount Payable.* All doctors of medicine becoming active members of this Association under the provisions of Section 1 of Chapter II of these By-Laws shall, as provided in Section 1 of Chapter II, pay to this Association the annual dues payable by active members for the period for which membership is obtained, except that the Council may, in its discretion, with respect to all new members who acquire membership after July 1 in each year, require payment of only one-half of the annual dues for said year. Such payment shall entitle such new member to all the rights of active membership in this Association until the end of the current calendar year.

Section 3.—Bequests, Legacies, Donations and Gifts

The Association may receive through the Council or for the benefit of the Association through any corporation which may be formed pursuant to the Constitution, such bequests, legacies, donations and gifts as the Council shall deem it proper and suitable to accept.

Section 4.—Funds and Moneys; Deposit and Withdrawal

All funds and moneys of the Association by whomsoever received shall be promptly forwarded to the Secretary-Treasurer of the Association and deposited by him in a depositary of the Association.

No demands or claims against the Association shall be paid and no funds or moneys of the Association withdrawn from any depositary thereof except upon written voucher approved by the signature of at least two members of the Auditing Committee or by a majority vote or written approval of a majority of all the members of the Executive Committee on check or draft signed by any two of the following: the Chairman of the Council; the Vice-Chairman of the Council (only in the absence of the Chairman); Chairman of the Auditing Committee; the Secretary-Treasurer.

Section 5.—Revolving Fund

A revolving fund in such amount as may from time to time be fixed by the Council shall be deposited with the Secretary-Treasurer from which fund immediate cash demands may be paid.

Section 6.—Surplus Funds From Journal and Publications

On authorization therefor by the House of Delegates or the Council, any surplus funds arising from the operation of the official journal or other publications of the Association may be applied and used for any purposes deemed suitable or may be delivered and paid over to any corporation which may be formed pursuant to, ... of the Constitution.

Section 7.—Contingency Fund

The contingency fund in the annual budget may not be in excess of twenty-five (25) per cent of the total amount of the approved budget.

CHAPTER XI.—REFERENDUM AND PETITION

Section 1.—Reference of Resolutions to Vote of Members

The House of Delegates may at any time, by a majority vote of those present, refer any resolution or motion pending before it to all of the active members of the Association for their vote for or against such resolution or motion. The Council may, by a two-thirds vote of all of its members and at any time within thirty (30) days after action was taken, refer any resolution or motion adopted by the House of Delegates to all of the active members of the Association for their vote for or against such resolution or motion. In addition, the Council may at any time, by a two-thirds vote of all of its members, submit any resolution or motion pending before it to all of the active members of the Association for their vote for or against such resolution or motion.

Section 2.—Form of Referendum: Arguments

The body referring any resolution or motion to the active members of the Association may, in the motion of reference, determine the form of the ques-

tion to be submitted. In the event the motion of reference does not determine the form of the question to be submitted, then the form thereof shall be fixed and determined by the Council. Written arguments for and against the resolution or motion, not exceeding 1000 words each, may be submitted by any member of the Association to the presiding officer of the referring body within fifteen (15) days of the vote of reference. Such presiding officer may choose one argument on each side and same shall then be printed and mailed with the ballots.

Section 3.—Manner of Voting; Time of Voting; Canvass

All references to the membership under this article shall be by mail ballot. The time within which each member shall cast his vote may be fixed in the motion of reference, and if not so fixed shall be fifteen days from the date of mailing ballots. Each vote must be in writing and the same must be placed in a sealed envelope bearing on the corner thereof the name of the voter. The envelope shall be mailed or delivered to the Secretary's office. The canvass thereof shall be made by a committee on referendums to be appointed, in the case of reference by the House of Delegates by the Speaker of the House, and in the case of reference by the Council by the Chairman of the Council. The Secretary shall deliver to such committee all ballots timely received, and the committee shall canvass the vote and report the results thereof immediately to the Secretary.

Section 4.—Effect of Referendum

To be considered adopted, any resolution or motion submitted to the membership by referendum shall require the same proportionate affirmative vote that such resolution or motion would have required to be adopted by the body (House of Delegates or Council) from which such resolution or motion was referred. Any resolution or motion submitted to a referendum and adopted shall have the same force and effect as though adopted in the body from which it was referred, and shall be considered as having been so adopted by such body.

Section 5.—Petitions

Any 100 active members or any component society may petition the House of Delegates or Council on any matter and such petition must thereupon be heard and considered at the next ensuing regular meeting of such body.

CHAPTER XII.—MISCELLANEOUS

Section 1.—Ethics

The principles of medical ethics as promulgated from time to time by the American Medical Association and by the California Medical Association are and shall be the principles of medical ethics of this Association and the component societies thereof, and shall regulate and govern all members thereof.

Interpretation of ethics about which any controversy may arise or exist shall be submitted to the Council of this Association, and its interpretation and ruling thereon shall be final.

Section 2.—Rules of Order

In the absence of any provision in the Constitution or these By-Laws, all meetings of the Association, of the House of Delegates, of the Council, and of committees shall be governed by the parliamentary rules and usages contained in the current edition of Roberts' "Rules of Order."

CHAPTER XIII.—AMENDMENTS

Section 1.—Amendments—Vote and Procedure

These By-Laws may be amended by the House of Delegates at any meeting of any session thereof by the affirmative vote of at least two-thirds of the qualified members thereof present and acting; provided, that any proposed amendment has been submitted in writing to the House of Delegates at least twenty-four hours previous to being voted upon.

CHAPTER XIV.—CORPORATIONS

To further aid in carrying out the objects of the Association the House of Delegates, at any meeting at any regular or special session thereof, may by a two-thirds vote of the membership thereof present and acting, authorize, empower and direct the Council to cause the formation and organization of one or more corporations under the laws of the State of California with such incorporators, name, purposes, county where the principal office for the transaction of business is to be located, first directors, the total number of shares, classes of shares, par value of any shares having par value, statement of the provisions, privileges and restrictions granted or imposed upon the respective classes of shares, or if the corporation be formed without capital stock, the authorized number and qualifications of its members, the different classes of members, if any, the property, voting and other rights of each class of members and the liability of each and all classes, to dues or assessments, and with such further provisions in the articles of incorporation thereof and with such by-laws as the Council shall prescribe, fix and determine; and the House of Delegates at any meeting of any regular or special session thereof may by a vote of two-thirds of the members thereof present and acting, authorize, empower and direct the Council to grant, assign, transfer, convey or deliver or cause to be granted, assigned, transferred, conveyed or delivered to any of such corporations upon the formation thereof or to applicants for health and accident or other insurance in or from any of said corporations at or prior to the formation thereof without any consideration therefor, such funds and property, real or personal, of this Association as the House of Delegates shall from time to time authorize or ratify.

CHAPTER XV.—REPEAL OF ALL EXISTING BY-LAWS

Section 1.—Repeal of Existing By-Laws

All chapters and all sections and parts of all chapters of the existing By-Laws of this Association are hereby repealed.

Council Meeting Minutes

Tentative Draft: Minutes of the 355th Meeting of the Council, August 21-22, 1948.

The meeting was called to order by Chairman Bruck in Room 210, Sir Francis Drake Hotel, San Francisco, at 10 a.m., Saturday, August 21, 1948.

Roll Call:

Present were President Askey, President-elect Kneeshaw, Speaker Alesen, Vice-Speaker Charnock, Councilors Ball, Crane, Henderson, Anderson, Ray, Bruck, Lum, Pollock, Green, Cherry, MacLean, Hoffman, Shipman, Bailey and Thompson, Secretary-Treasurer Garland and Editor Wilbur. A quorum present and acting.

Present by invitation were Legal Counsel Hassard, Executive Secretary Hunton, Assistant Executive Secretary Wheeler, Field Secretary Clancy, Public Relations Counsel Whitaker, county society executive secretaries Waterson of Alameda County, Donovan of Santa Clara County, and Kihm of San Francisco County, and Ben H. Read, Executive Secretary of the Public Health League of California.

Present by invitation during portions of the meeting were Dr. Malcolm Merrill of the State Department of Public Health, Dr. Forrest G. Bell of the Veterans Administration, Dr. Robertson Ward, president of the San Francisco County Medical Society and C.M.A. Delegate to the A.M.A.; Dr. John Upton, chairman of the C.M.A. Blood Bank Commission; Dr. Carroll B. Andrews, director of postgraduate activities; Dr. C. L. Cooley, Secretary, and William M. Bowman, executive director of California Physicians' Service, and the Hon. Sam L. Collins, Speaker of the Assembly of the California State Legislature.

1. *Minutes:*

(a) On motion duly made and seconded, minutes of the 354th meeting of the Council, held June 5-6, 1948, were approved.

(b) On motion duly made and seconded, minutes of the 210th meeting of the Executive Committee, held July 21, 1948, were approved.

2. *Membership:*

(a) A report of membership as of August 20, 1948, showing 8,997 paid and 532 delinquent members, was received.

(b) On motion duly made and seconded, two members whose 1947 dues had been received since June 5, 1948, were voted reinstatement as active members.

(c) On motion duly made and seconded, 55 members whose 1948 dues had been received since June 5, 1948, were voted reinstatement as active members.

(d) On motion duly made and seconded in each case, three applicants for Associate Membership were voted membership as Associate Members. They were:

J. B. Askew, San Diego County.
Robert P. Quirmbach, Santa Clara County.
Judith T. Garber, Ventura County.

(e) On motion duly made and seconded in each case, three applicants were voted membership as Retired Members. They were:

Chester F. Johnson, Alameda County.
Stanley H. Mentzer, San Francisco County.
Deon A. Crew, San Luis Obispo County.

(f) On motion duly made and seconded in each instance, three applicants were voted membership as Life Members. They were:

William H. Barnes, Alameda County.
J. Emit Cox, Fresno County.
C. H. Montgomery, Los Angeles County.

(g) The committee appointed at the last previous Council meeting to prepare rules for the reduction of dues in special cases (Kneeshaw, chairman; Charnock, Anderson) presented its report, which, after discussion, was regularly moved for adoption, seconded and favorably voted. This report provides:

(Legal counsel preparing specific language, for approval by committee members and subsequent Council approval.)

(h) The Executive Secretary reported that a canvass of the component county societies had not produced any members eligible for presentation of an emblem to honor such members for fifty years of membership. A sample emblem was exhibited but no action taken.

3. *Financial:*

(a) A report of bank balances as of August 20, 1948, was received and ordered filed.

(b) A balance sheet as of July 31, 1948, was received and ordered filed.

(c) A report of income and expenditures for July, 1948, first month of the current fiscal year, was received and ordered filed.

(d) The Executive Secretary reported that, acting on previous instructions from the Trustees of the California Medical Association, he had purchased $10,000 par value U. S. Treasury 2½ per cent bonds, maturing 1967-72.

(e) The Council committee on investment of funds (Kneeshaw, Ray) recommended that current surplus funds of the Association be invested in 91-day U. S. Treasury bills on a monthly revolving fund basis which would make needed cash available each month and permit the earning of a little less than 1 per cent per annum on invested funds. On motion duly made and seconded, this report was accepted and the Secretary-Treasurer authorized to purchase such bills.

4. *Constitution and By-Laws:*

The Chairman reported that numerous suggestions had been made for the membership of a committee to review the Association's Constitution and By-

Laws, as directed by the 1948 House of Delegates. He listed a number of names which had been proposed and, after discussion and with the consent of the Council, named the following as members of this Committee: Sam J. McClendon of San Diego, chairman; Carl L. Mulfinger and Richard O. Bullis of Los Angeles, Leslie Magoon of Santa Clara County and John W. Cline of San Francisco County.

5. *State Department of Public Health:*

(a) Dr. Bruck reported on a mailing he had made as part of a survey of the needs for caring for chronic illnesses and a similar mailing sent by others to county health officers, in which he believed leading questions were asked. Returns from these mailings are not yet complete but will be presented to a meeting of the State Department of Public Health's committee to study chronic diseases at a meeting scheduled for September 13-14. Dr. Bruck is a member of this committee.

(b) Dr. Malcolm Merrill, representing Dr. Wilton L. Halverson, State Director of Public Health, reported that special studies are being made on diabetes, heart disease and chronic alcoholism, the results to be presented at the meeting of the committee on chronic diseases.

He also stated that the State Department of Public Health has secured the services of a physician to cooperate with the blook banks, laboratories, etc., throughout the state on the technical aspects of blood banking, particularly as to grouping and typing.

Dr. Merrill summarized the present situation in poliomyelitis, pointing out that 1948 appears to be headed toward becoming the second worst year in the state's history in number of polio cases. There is a leveling off at present, which should presage a break in the polio situation in October or November.

(c) Dr. Askey reported that Doctors Cullen Ward Irish, Chairman; Hall G. Holder, Malcolm H. Merrill, George H. Houck and John Martin Askey had been appointed as members of the C.M.A. special committee on alcoholism and asked the Council to determine the scope of the committee's studies. It was agreed that the first objective of this committee should be to study and correlate the activities of various agencies in the state which are already at work on this problem.

(d) A letter from a member was read in which he complained of the manner in which he had been subpoenaed to appear in a court action, the subpoena being served by a representative of the State Department of Public Health. He criticized the manner in which this matter was handled, particularly as to the inconvenience caused him and the fact that no provision had been made for meeting his travel expenses. Legal counsel pointed out that this was a criminal case and that the subpoena originated with the district attorney of the county involved and not with the State Department of Public Health. It was agreed that assistance should be given by legal counsel in attempting to secure reimbursement for the member's expenses in answering this subpoena.

6. *California Physicians' Service:*

(a) Dr. C. L. Cooley, Secretary of California Physicians' Service, reported that C.P.S. has adopted stricter underwriting provisions which have tended to slow down its sales program and worked toward improving the servicing provisions of its present program, with results which are highly satisfactory to the Board of Trustees. Complete authority has been granted to Dr. William L. Bender, chairman of the fee schedule committee, to work for a revision of the present fee schedule and a new schedule is expected in the near future. Changes are being made in one of the service forms (Form 9) so that the beneficiary member will hereafter certify to his income being below the income ceiling.

Mr. William M. Bowman, executive director of C.P.S., distributed financial statements covering C.P.S. operations for the four months ended July 31, 1948, and a balance sheet as of July 31. Operations for this period showed a gain of $216,297 in the stabilization fund reserve, bringing the balance at July 31, 1948, to $401,585. Copies of these reports are to be furnished to members of the Council regularly, as well as to county societies to be read at next regular meeting of societies.

(b) Mr. Hunton reported that letters had been sent to approximately 125 hospitals asking their cooperation with C.P.S. in the matter of accepting prorated fees for radiological and pathological work and that only *two* replies had been received, both declining to accept anything less than their standard fees. It was advised that copies be sent to the regional hospital conferences, with a renewed request for cooperation.

7. *Hospitals:*

(a) Mr. Hassard reviewed the opinion issued by the State Attorney General which held that hospitals employing professional personnel and billing patients for their services without regard to the emoluments paid the professional staff were violating the corporate practice sections of the medical practice act. The Association of California Hospitals has instructed its legal counsel to work with Mr. Hassard in preparing forms of specimen contracts to cover the working arrangements of radiologists, pathologists and other physicians who may be affected by this ruling. On motion duly made and seconded, Mr. Hassard was voted authority to proceed in working with legal counsel for the hospitals in drafting the proposed specimen contracts.

(b) Dr. Bruck presented a hospital survey made in Contra Costa County and a series of questions asked by officers of the Contra Costa County Medical Society. It was regularly moved, seconded and voted to refer this matter to the standing Committee on Hospitals, Dispensaries & Clinics and to notify the county society and Dr. George Degnan to that effect.

8. *Veterans' Administration:*

Dr. Forrest G. Bell, deputy regional medical director of the Veterans' Administration, appeared be-

fore the Council by invitation. He stated that regional diagnostic clinics were proposed to be established in order to give patients comparable facilities to those in V.A. hospitals. San Diego has been selected as a pilot in this program; local physicians are to be employed on a part-time basis, at $25 for a two-hour period of duty, or $50 for shorter periods for specialists. He stated that the Veterans' Administration has no intention of decreasing the out-patient care program now being carried on under the V.A.-C.P.S. contract; the V.A. budget, he said, calls for 25 per cent of all pension examinations to be carried on outside V.A. hospitals and 75 per cent of all payments for medical services to be made to private physicians.

In response to questions, Dr. Bell stated that in no event were non-service connected disabilities entitled to care in regional offices; also, that the Veterans' Administration in the Branch 12 area has 3,000 of its cases being cared for in Army and Navy hospitals under contract arrangements.

Following Dr. Bell's retirement, Doctors Kneeshaw, Thompson and the secretary were appointed a committee to draw up proposed resolutions on the subjects of regional clinics and the contracting for care for V.A. patients. Upon presentation and after discussion, the following two resolutions were regularly moved for adoption, seconded and unanimously approved:

COUNCIL RESOLUTION ON VETERANS ADMINISTRATION CLINICS

Whereas, The provision of the best type of medical care to all veterans with service-connected disabilities is a prime interest of the medical profession, and

Whereas, The Council of the C.M.A. sincerely believes that such care may best be provided under conditions as nearly as possible identical with those obtaining in regular private medical practices, and

Whereas, Complete facilities and arrangements for such care are and have been available for over two years in California under the C.P.S.-V.A. program, and

Whereas, There is considerable doubt as to the need of establishing additional expensive treatment clinics; now, therefore, be it

RESOLVED: That the Council of the C.M.A., acting on behalf of all its members and in the interest of sound medical care to all veterans, respectfully requests the V.A. to review carefully and reconsider its recently announced program to establish "diagnostic and/or treatment clinics" in its regional and subregional offices; and be it further

RESOLVED: That members of this Association give every aid to the V.A. in the provision of sound medical care to veterans in this state, under existing arrangements.

COUNCIL RESOLUTION ON VETERANS ADMINISTRATION HOSPITALS

Whereas, It is reliably reported that about 75 per cent of the cases admitted to V.A. Hospitals are *not* suffering from *service-connected* injuries or disorders, and

Whereas, Many of these cases are referred to (or "farmed out" to) Army or Navy Hospitals, thereby increasing the apparent shortage of military service physicians; now, therefore be it

RESOLVED: That the practice of admitting private patients with *non*-service connected disabilities to Veterans Hospitals is a potential source of serious delay in the handling of patients with service-connected ailments, is an undue hardship on the taxpayer, is highly discriminatory, and should be discontinued in the case of all those persons who are able to provide their own hospital care; and be it further

RESOLVED: That copies of this resolution be transmitted to the Veterans Administration, the A.M.A., the other State Medical Associations and our representatives in Washington.

It was agreed that copies of these resolutions should be forwarded to the Veterans Administration, the surgeons general of the Army and Navy, the Secretaries of Defense, Army and Navy, the American Medical Association, the secretaries of state medical associations and the members of Congress serving on military affairs committees.

9. *Blood Banks:*

Dr. Robertson Ward, as a Delegate to the A.M.A., reported on the blood bank business before the 1948 A.M.A. House of Delegates. The House of Delegates approved the report of the A.M.A. Board of Trustees in which the approval in principle of the American Red Cross blood bank program was reaffirmed. Following a meeting of a reference committee at which a Red Cross representative had expressed a feeling of difficulty with the operations of some local blood banks and had stated that the Red Cross intended to proceed as rapidly as possibly to take over all local blood banks, the reference committee brought in a report, later accepted by the House of Delegates, in which further clarification was given the principles upon which A.M.A. approval was based. Dr. Ward considered this a forward step in the relationship of the profession with the Red Cross program.

Dr. John Upton, chairman of the CMA Blood Bank Commission, reported that newspaper files indicated a growing resentment, nationwide, against the Red Cross blood bank program. He reported that the commission is proceeding without definite instructions as to the extent of its authority, that additional blood banks are needed in some areas of California and that the commission is striving to assure a supply of blood to all areas of the state. An attempt is being made to start blood banks in Santa Barbara, Bakersfield, Fresno and one northern city as a part of this program. There are now in the state five community type blood banks, nine in county hospitals, fourteen in private hospitals and four new banks either operating or preparing to operate. It was agreed that a letter be sent to all county medical societies telling of the availability of the services and advice of the blood bank commission.

10. *California Medicine:*

(a) On motion duly made and seconded, it was voted to elect Doctor Maurice Sokolow to the Editorial Board of CALIFORNIA MEDICINE to succeed Doctor Mayo Soley, who has moved from the state.

(b) On the question of accepting liquor advertising, it was moved, seconded and voted that due to present conditions such advertising should not be accepted.

(c) On motion duly made and seconded, it was voted to inform the advertising committee of CALIFORNIA MEDICINE that institutional advertising should not be accepted from advertisers who did not have products acceptable for advertising in the journal.

(d) On motion duly made and seconded, William C. Mumler and Clifford Cherry of Los Angeles were elected members of the advertising committee, to counsel particularly on matters concerning Southern California advertising prospects.

(e) On the question of repeated use of physicians' names in institutional advertisements appearing in the journal, the advertising committee was asked to make review and recommendations.

11. *C.M.A. Section on Neuropsychiatry:*

The chairman read a letter from the Section on Neuropsychiatry, in which it was asked that the name of the section be changed. It was pointed out that the House of Delegates has sole authority in such cases and that the section officers be so notified.

12. *Recess:*

At this point, 5:15 p.m., the Council recessed until 9:30 a.m. Sunday, August 22, 1948.

13. *Reconvention:*

The Council reconvened at 9:30 a.m., Sunday, August 22, 1948, in Room 210 of the Sir Francis Drake Hotel.

14. *Roll Call:*

Present were all Officers, Councilors and Council members ex-officio. Present by invitation were Messrs. Hunton, Hassard, Read, Clancy, Wheeler, Whitaker, Kihm and Venables (executive secretary, Kern County Medical Society), Mr. W. M. Bowman of C.P.S. and Dr. Dwight H. Murray, chairman of the Committee on Public Policy & Legislation.

15. *Committee on Industrial Practice:*

On behalf of the Committee on Industrial Practice, Mr. Hunton and Dr. Pollock (member of the Committee) presented the proposed schedule of fees for industrial compensation cases. Mr. Hunton stated that the Industrial Accident Commission of the State of California had held public hearings on June 7 and June 10, 1948, on the application of the California Division of the Western Orthopedic Association for an increase in specific fees in the existing fee schedule. At the invitation of the two members of the Industrial Accident Commission who served as a committee on this application, the Association appeared and Mr. Hunton presented a three-point statement: (1) that the fee schedule should be attacked as a whole and not piecemeal, (2) that the Committee on Industrial Practice was preparing a new proposed complete fee schedule which would be ready for presentation to the Commission by September 1, 1948, and (3) that if the Commission wished to establish a "study committee" as it had done several years earlier, such committee be limited in size and be composed of a suggested three representatives of medicine, three of employers or their insurance carriers and one or two members of the Commission as referees.

After discussion it was regularly moved, seconded and voted that the Committee on Industrial Practice be authorized to proceed with the presentation of the proposed fee schedule to the Industrial Accident Commission.

16. *Public Relations:*

Mr. Whitaker discussed several propositions which will appear on the November general election ballot and suggested that the physicians of the state be urged to take an active interest in them. This report was informative and no action was taken.

Mr. Whitaker also reported that he had been asked to utilize the "California Caravan" radio program for detailing the history of the development of blood banks, possibly in connection with the annual meeting of the Radiological Society of North America. It was regularly moved, seconded and voted that Mr. Whitaker be authorized to proceed in meeting this request.

It was also regularly moved, seconded and voted that the Blood Bank Commission continue its present program under provisions of the existing budget and that any contemplated additional expenditures be presented to the Council for approval.

17. *Employees' Retirement Program:*

Dr. Charnock presented the recommendation of his special committee (Charnock, Alesen, John W. Cline) that retirement annuity insurance be purchased for Association employees with five or more years of employment, annuities to begin at age 65 at the rate of 25 per cent of annual wages, with a maximum of $200 monthly to any one employee. Dr. Kneeshaw suggested that such insurance be purchased by the Association for male employees but that the Association carry its own insurance for female employees by purchasing U. S. Treasury bonds each month for serial maturity and payment at a later date.

It was regularly moved, seconded and voted that the committee's report dealing with male employees be put into effect at once and that the remaining portion of the report be re-referred to the committee, Doctors Kneeshaw and Askey being added to the committee.

18. *Public Policy and Legislation:*

Dr. Dwight H. Murray reported that Hon. Ernest R. Geddes, a member of the State Assembly, was suffering from an illness and it was regularly moved, seconded and unanimously voted that the Secretary address a letter to him, conveying the concern of the Council over his condition and expressing wishes for his speedy recovery.

Mr. Read, Mr. Clancy and Mr. Hassard reported on various candidacies and propositions which will appear on the November ballot. No action taken.

19. *Legal Department:*

(a) Mr. Hassard reported on a memorandum issued by deputies in the State Attorney General's office, holding that county hospitals were eligible to receive federal funds as grants-in-aid for hospital construction if such county hospitals make their facilities available to all residents of the county regardless of ability to pay for such services. He stated the Attorney General has reviewed this memorandum and has ordered a complete review of the entire matter by the deputies involved.

(b) Mr. Hassard also reported on suits which have been threatened against the officers of the San Diego County Medical Society by legal counsel for several physicians who have failed of election to the society. On motion duly made and seconded, it was voted to authorize legal counsel to lend all possible aid and assistance to the San Diego County Medical Society in this matter.

(c) Mr. Hassard reported on a Chicago meeting (August 19 and 20, 1948) between the Blue Cross Commission and the Blue Shield Commission, at which the proposition of forming a joint association, with each organization maintaining its own identity, was considered. Also discussed was the possibility of forming a joint corporation for the purpose of issuing indemnity insurance contracts for medical, surgical and hospital service to employees of interstate organizations, with local plans to administer the program in their own areas up to the limit of their own programs. It has been proposed that an Illinois corporation be formed, with capital of $500,000, voting stock to be held by the Blue Shield and Blue Cross plans. On motion duly made and seconded, it was voted that the Council approve these proposals and recommend to the C.P.S. Board of Trustees that they give their approval.

(d) Mr. Hassard stated that the prepaid medical care plans in the western states had held a meeting in Chicago on June 19 and had voted to form a western conference of medical service plans, provided six or more of the plans in the area approved such formation. More than six plans have now ratified this arrangement and such a conference is in process of formation.

20. *Medical Ethics:*

In accordance with action previously taken, the chairman called for nominations for a special committee to codify the principles of medical ethics. This committee was named as Wilbur Bailey, Chairman; Donald A. Charnock and Dell Lundquist.

21. *Ross-Loos Clinic:*

The Chairman read a letter from Doctor H. Clifford Loos, outlining the application of the Ross-Loos Clinic for approval to use the seal of the A.M.A. Council on Medical Service. On motion duly made and seconded, the amendment duly made, seconded and voted, it was regularly voted that the Secretary advise the A.M.A. Council on Medical Service that it has no objection to the consideration of the Ross-Loos application by that Council provided the rules of the Council have been met and that since the Los Angeles County Medical Association has given its approval, the Council on Medical Service be urged to consider and expedite the Ross-Loos application.

22. *Physician Membership in Lay Health Groups:*

Dr. Bailey introduced a resolution proposing the adoption of a statement of policy by the Association relative to the membership of physicians in lay health groups which advocated or permitted their officials to advocate a system of socialized medicine. It was regularly moved, seconded and voted to refer this matter to a special committee for study and report back to the next Council meeting. The Chairman announced this committee as John W. Cline, Chairman; Lewis A. Alesen, E. Vincent Askey, H. Gordon MacLean and Dwight L. Wilbur.

23. *American Academy of Pediatrics:*

A request from the American Academy of Pediatrics for publication in CALIFORNIA MEDICINE of a survey made in California was presented and it was regularly moved, seconded and voted that the matter be referred to the executive board of the Editorial Board and the Executive Committee of the Association.

24. *Committee on Medical Economics:*

Dr. MacLean, chairman of the Committee on Medical Economics, requested that representatives of the C.M.A. and the Association of California Hospitals be named as members of a joint committee of these organizations, the Blue Cross plans and C.P.S. to study matters of mutual interest. It was agreed that such representatives be named.

Dr. MacLean also requested authority for his committee to proceed with its investigation of delinquent accounts and other items pertinent to a study of individual physician-patient relationships. On motion duly made and seconded, it was voted that the committee proceed with this work and that expenses up to $5,000 be approved for this study. (Of an earlier appropriation of $5,000 for this study, $2,326.96 was expended and the balance returned to the general fund.)

25. *California Ambulance Association:*

A request from the California Ambulance Association for counsel in connection with the establishment of ambulance standards was read and it was agreed

that representatives of the Association should meet with ambulance representatives and give such assistance as possible.

26. *Time and Place of Next Meeting:*

After discussion it was agreed that the next Council meeting should be held in Los Angeles on November 13 and 14, 1948.

27. *Adjournment:*

There being no further business to come before the meeting, it was adjourned.

EDWIN L. BRUCK, M.D., *Chairman.*
L. HENRY GARLAND, M.D., *Secretary.*

In Memoriam

CARSON, GEORGE RYCKMAN. Died in San Francisco, June 15, 1948, age 72, after a long illness. Graduate of the Cooper Medical College, San Francisco, 1901. Licensed in California in 1901. Doctor Carson was a retired member of the San Francisco County Medical Association, and the California Medical Association.

✤

COMSTOCK, DANIEL DELOS. Died in Oakland, Maryland, August 29, 1948, aged 68, of a heart attack. Graduate of the American Medical Missionary College, Battle Creek, 1906. Licensed in California in 1910. Dr. Comstock was a member of the Los Angeles County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

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DOWLING, STANLEY WALDO. Died in San Francisco, June 25, 1948, at age 60, of appendicitis and peritonitis with cardiovascular complications. Graduate of the Cooper Medical College, San Francisco, 1912. Licensed in California in 1913. Doctor Dowling was a member of the Santa Cruz County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

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FINNERTY, EDWARD JAMES JOSEPH. Died in Sonoma, August 15, 1948, aged 59, of a heart attack. Graduate of the University of Toronto Faculty of Medicine, Ontario, 1911. Licensed in California in 1911. Dr. Finnerty was an associate member of the Sonoma County Medical Society and the California Medical Association.

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GILMAN, PHILIP KINGSNORTH. Died in San Francisco September 7, 1948, aged 69, of a coronary failure. Graduate of Johns Hopkins University School of Medicine, Baltimore, 1905. Licensed in California in 1916. Dr. Gilman was a member of the Marin County Medical Society, the California Medical Association, and the American Medical Association.

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HERRICK, ALBERT BENJAMIN, JR. Died in Santa Rosa, August 22, 1948, aged 60, of a heart attack. Graduate of Oakland College of Medicine and Surgery, Oakland, 1913. Licensed in California in 1914. Dr. Herrick was a member of the Sonoma County Medical Society, the California Medical Association, and the American Medical Association.

HYDE, CLARENCE ELMER. Died in San Jose, June 6, 1948, age 64, after an illness of two years. Graduate of Columbia University College of Physicians and Surgeons, New York, 1909. Licensed in California in 1911. Doctor Hyde was a retired member of the San Francisco County Medical Association, and the California Medical Association.

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JORDAN, PHILIP JEROME. Died in San Jose, September 1, 1948, aged 37. Graduate of Stanford University School of Medicine, San Francisco, 1938. Licensed in California in 1938. Dr. Jordan was a member of the Santa Clara County Medical Society, the California Medical Association, and the American Medical Association.

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MATTISON, CHARLES WESLEY. Died in Temple City, August 26, 1948, aged 74. Graduate of the University of Illinois College of Medicine, Chicago, 1904. Licensed in California in 1918. Dr. Mattison was a retired member of the Los Angeles County Medical Association and the California Medical Association.

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MURRIETA, ALFRED JOHN. Died in Los Angeles, August 6, 1948, aged 72. Graduate of the University of Southern California School of Medicine, Los Angeles, 1899. Licensed in California in 1900. Dr. Murrieta was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

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PARETZKY, MEYER. Died in Los Angeles, May 17, 1948, at age 54. Graduate of Kharkow Medical Institute, Kharkow, Ukrainian S. S. R., 1917. Licensed in California in 1923. Doctor Paretzky was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

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PEARSON, BRUCE REED. Died in Salt Lake City, August 16, 1948, aged 44, of a heart attack. Graduate of the Stanford University School of Medicine, San Francisco, 1932. Licensed in California in 1932. Dr. Pearson was a member of the Stanislaus County Medical Society, the California Medical Association, and the American Medical Association.

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PHILLIPS, ALBERT DANA, JR. Died in Goose Bay, Labrador. December 9, 1947, aged 42, in an airplane crash. Graduate of Syracuse University College of Medicine, 1930. Licensed in California in 1931. Dr. Phillips was a member of the Sacramento County Medical Society, the California Medical Association, and the American Medical Association.

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THELEN, HENRY MUIR. Died in Berkeley, July 26, 1948, at age 32, of rheumatic heart disease. Graduate of Johns Hopkins University School of Medicine, Baltimore, Maryland, 1941. Licensed in California in 1942. Doctor Thelen was a member of the Solano County Medical Society, the California Medical Association, and American Medical Association.

✤

THOMPSON, HAROLD A. Died in San Diego, July 31, 1948, aged 64, of hypertensive heart disease. Graduate of the University of Southern California School of Medicine, Los Angeles, 1906. Licensed in California in 1906. Dr. Thompson was a member of the San Diego County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

VISSCHER, LOUIS GEORGE. Died in Los Angeles, July 15, at age 84. Graduate of Julius-Maxmilians-Universität, Medizinische Fakultät, Würzburg, Bavaria, 1891. Licensed in California in 1898. Doctor Visscher was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

✤

WALT, RICHARD WILLIAM. Died in Los Angeles, August 16, 1948, aged 35, in an automobile accident. Graduate of the University of Southern California School of Medicine, Los Angeles, 1942. Licensed in California in 1942. Dr. Walt was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

Philip Kingsnorth Gilman

"By his works ye shall know him"

The medical profession received the announcement of the death of Dr. Philip K. Gilman with deepest regret. There now exists a void where once was a source of strength upon which so many relied.

Following a mild distress five days previously, while occupied in State hospital investigations, Dr. Gilman was under medical care when, on the morning of September 7, 1948, the end came suddenly from a coronary occlusion.

Dr. Gilman was probably personally acquainted with more physicians and knew more laymen of prominence than most of his contemporaries. Men in all important walks of life sought his advice almost daily, even through the last three years while he was engaged in the study of hospital needs throughout the state for the Department of Health. His judgment, with his humanitarianism was always available for any problem. These services he rendered will long be remembered.

Life began for Doctor Gilman in Oakland 69 years ago. His youth was rich in the opportunity of learning to enjoy the outdoor life. Following an academic degree at Stanford University, he studied medicine at Johns Hopkins Medical School. Upon graduation in 1905, he answered a call for medical work in Manila where he spent several years as surgeon and teacher. He again became a resident of California in 1916, joined the faculty of Stanford Medical School and engaged in the private practice of surgery in San Francisco. For many years he was Clinical Professor of Surgery at Stanford. The first world war found him a lieutenant in the Navy Reserve attached to Naval Base Hospital No. 2, which saw service in Scotland. He never lost his attachment for the Navy and, in the following years, he rose in rank until, in 1939, he was appointed Captain. He accepted active duty in June of 1941, served under the District Medical Officer of the Twelfth Naval District, was Medical Procurement Officer, Executive Officer at Naval Hospital. Oakland, and Assistant District Medical Officer. He was transferred to the honorary retired list, for age, in 1943 and retained on active duty until April, 1945.

It was upon his return to private practice after the first world war that Doctor Gilman gave so much of himself to his profession and the community. Being public spirited, he responded to any request to serve. He gave of his time to his county society, the State society, the Community Chest, the California Physicians' Service. He coordinated the thoughts and efforts of a number of public spirited physicians in San Francisco into a local organization which, soon after, developed into the Public Health League of California.

Doctor Gilman served his county society as a member of the Board of Directors for nine years, actively represented that organization in the state society House of Delegates for five years, and was president of it in 1936. In all these posts his faithfulness was steadfast and ability outstanding.

He served on the council of the state association for eight years and was chairman from 1940 to 1946. It was while holding the position of chairman that his judgment, his ability to sense the right action and his good influence over physician and layman came to the fore and rendered such valuable service to the society. Many of the policies adopted then are accepted as standards in the society today.

The state society tendered the highest honor to Dr. Gilman by electing him president-elect in May, 1944, and president May 7, 1945.

Other services were rendered to his profession without stint as in the Pacific Coast Surgical Society and the National Council of Presidents of State Medical Societies.

Dr. Gilman was a great physician, a skillful surgeon, an excellent diagnostician. He was always considerate of the patient, kindly, gentle, reassuring. To be under his care was to be a faithful disciple, happy to follow his advice. He exemplified the true spirit of Hippocrates. He was a real teacher, imparting clearly his knowledge to his students, who invariably returned to him for advice and counsel.

The optimism and vivacity of youth retained by Dr. Gilman to the last was, in no small part, due to the pleasure of participating regularly in the plays of the Bohemian Club in the Bohemian Grove. He accepted his part and read his lines with a voice and spirit that carried all on to success.

A sterling character, graciousness, gentleness, generosity beyond the average, fearlessness, and a determination to give his all to improve the economies of his profession, to protect the ill from over-zealous sociologists, to preserve the freedom of living we have enjoyed, were attributes of Dr. Gilman. His life is a model to be studied and emulated. While bowing in reverence to the passing of a true friend, let us offer thanks for the privilege of living and working with a great citizen. E. J. B.

NEWS and NOTES

NATIONAL • STATE • COUNTY

ALAMEDA

Dr. David B. Wilson last month became assistant medical director of Alameda County, filling a post left vacant when Dr. W. W. Stadel resigned to accept appointment as superintendent of San Diego County Hospital. Dr. Wilson formerly was with the U.S. Public Health Service in administration of a national hospital survey and construction program.

LOS ANGELES

The University of Southern California Medical School was one of four medical schools sharing in a total of $16,000 in grants-in-aid awarded by the National Vitamin Foundation to support vitamin research. Dr. E. Geiger, professor of pharmacology and toxicology at the school, is being assisted in investigations to determine the effects of time elements on the utilization of water soluble vitamins.

* * *

The American College of Surgeons will holds its 34th Clinical Congress in Los Angeles October 18-22. An extensive program of surgical operations, some of which are to be transmitted by television to convention headquarters in the Biltmore hotel, are being prepared by personnel and surgeons at 24 hospitals in the metropolitan area.

* * *

Dr. Burrell O. Raulston, dean of the University of Southern California Medical School, has been appointed a member of the National Advisory Heart Council by Leonard A. Scheele, Surgeon General of the U.S. Public Health Service. The advisory council will serve the National Heart Institute which was created in the National Heart Act passed by Congress and approved by the President last June. Under the Act the Public Health Service will set up a program to include the conduct of research, financial aid to institutions for research and training of professional personnel, fellowships for individual scientists, and grants-in-aid and technical assistance to the states for heart disease control services.

* * *

Dr. William P. Longmire, Jr., professor of surgery in the Johns Hopkins University Medical School, has been appointed professor of surgery in the School of Medicine at the University of California at Los Angeles. Dr. Longmire received his M.D. degree at Johns Hopkins in 1938.

NAPA

Dr. Kenneth Haworth, who recently resigned as health director of Humboldt and Del Norte counties, has been appointed health director of Napa County.

SAN BERNARDINO-RIVERSIDE

Initial steps in the organization of the Academy of General Practice of the San Bernardino and Riverside counties were taken recently at a meeting of physicians in general practice in the two counties. Committees were chosen to form a constitution and by-laws and present nominations for officers of the organization, which will be a unit of the American Academy of General Practice. Purposes of the Academy, as explained by Dr. C. T. Halburg, who is a member of the board of directors of the California Academy of General Practice, are to promote high standards in the general practice of medicine and surgery, and to assist in providing postgraduate study courses for general practitioners.

SAN FRANCISCO

Dr. Daniel G. Morton, professor of obstetrics and gynecology at the University of California Medical School, has been named a director of the American Board of Obstetrics and Gynecology.

* * *

Appointment of Dr. Karl F. Meyer, director of the Hooper Foundation, University of California, as one of the ten directors of the recently formed Arthritis and Rheumatism Foundation, has been announced by Dr. W. Paul Holbrook, president of the foundation. Purpose of the foundation is to promote a united nation-wide attack on arthritis and other rheumatic diseases through efforts of lay and medical leaders.

* * *

Stanford University School of Medicine announces that the 1948 Jacob Gimbel Lectures on Sex Psychology will be held October 18, 20, and 22 in Lane Hall, San Francisco, and will be followed by the Harzstein Medical Lectures October 25, 26 and 28 at the same place. All lectures will begin at 8:15 p.m. The Gimbel lecturer will be John C. Whitehorn, M.D., professor of psychiatry and director of the department of psychiatry, Johns Hopkins University, whose subject will be "Sex Behavior and Sex Attitudes in Relation to Emotional Health." Robert E. Gross, M.D., Ladd professor of children's surgery at Children's Hospital, Boston, will deliver the Herzstein lectures. The subjects of his lectures will be "Surgery in the Early Months of Life," "Surgical Treatment of Congenital Cardiovascular Disease," and "The Experimental Laboratory in Relation to Pediatric Surgery."

Attendance at all lectures is open to members of the medical profession, including practitioners and students, and other interested persons.

The Western Orthopedic Association will hold its annual meeting in the St. Francis Hotel, San Francisco, November 3, 4 and 5.

YUBA

Dr. Stanley J. Smiley, formerly of Sacramento, has been appointed county physician of Yuba County to take the place of Dr. James J. Hamilton, who last month resigned that post to enter private practice.

GENERAL

Druggists and the medical profession are being urged by the Federal Security Agency's Food and Drug Administration to return all stocks of Siliform Ampuls to the manufacturer, the Heilkraft Medical Company, Boston, Mass. This injectable drug, which should be sterile, is potentially dangerous since samples collected on the market contain living organisms, the Food and Drug Administration said. Siliform is injected by some physicians and osteopaths in the belief it will relieve patients suffering with rheumatism as

claimed by the manufacturer, according to the government agency. The article was shipped to 37 states from Maine to California and later was redistributed by wholesalers who cannot trace many of their sales. Some going back as far as 1946 have been found on the market. These ampuls may be in the hands of doctors, hospitals, clinics, and retail and wholesale druggists, it was said.

* * *

Two grants to finance special cancer projects in California were made recently by the U. S. Public Health Service through the California State Department of Public Health. The University of California Medical School was awarded $43,320 for research and training in the cytological smear technique for diagnosis, and a second grant of $9,275 will be administered jointly by the State Department of Health and the Cancer Commission of the California Medical Association to finance seminars by cancer specialists for members of county medical societies in non-metropolitan areas.

* * *

The 27th annual Hospital Standardization Conference will be held at the Biltmore Hotel, Los Angeles, from October 18 to 22, in conjunction with the 34th annual Clinical Congress of the American College of Surgeons, according to an announcement by Dr. Malcolm T. MacEachern, associate director and chairman of the administrative board. Hospital authorities from all parts of the United States and Canada will participate.

* * *

Applications to take a written qualifying test in 1950 as a first step for certification by the American Board of Ophthalmology are now being accepted from candidates, according to an announcement by the Board, and will be considered in the order received until the quota is filled. Registration for the test to be held in 1949 already is closed. Address of the Board is Cape Cottage, Maine.

* * *

Three prizes—$500, $300, and $200—are being offered by the American Urological Association for essays on the result of clinical or laboratory research in urology. Competition is limited to urologists who have been in that specific practice for not more than five years and to residents in urology in recognized hospitals. Essays must be in the hands of the secretary of the association, Dr. Thomas D. Moore, 899 Madison Ave., Memphis 3, before February 15, 1949. Full particulars may be had by writing to Dr. Moore.

The American Goiter Association again offers the Van Meter Prize Award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association which will be held in Madison, Wisconsin, May 26, 27 and 28, 1949. The competing essays, which may cover either clinical or research investigations, may be sent to the corresponding secretary, Dr. T. C. Davison, 207 Doctors Building, Atlanta 3, Georgia, not later than March 15.

* * *

The American College of Physicians will conduct its 30th Annual Session in New York City, March 28 through April 1, 1949. Early announcement of the date of the meeting was made, it was explained, so that other organizations might avoid conflicting dates in setting the time for their meetings.

* * *

Veterans Administration has immediate openings for at least 100 young doctors interested in taking residency training in psychiatry or neurology or both, Dr. Paul B. Magnuson, chief medical director, announced recently.

VA hospitals offering these residencies are situated in almost every section of the country. In the Branch 12 area (California, Nevada, Arizona and Hawaii) approximately 20 young doctors will be needed in the VA hospitals at Palo Alto and Los Angeles. All are under supervision of the deans' committees, mostly composed of members of university faculties of Class "A" medical schools.

In general, these residencies cover a three-year program of specialty training, although one and two-year programs also are available at most of the hospitals. Those interested may obtain information and application forms by writing the Chief Medical Director, Veterans Administration, Washington 25, D. C.

* * *

The Second California Rural Health Conference, sponsored by the California Committee on Rural Medical Health, will be held October 16 at the Hotel Senator, Sacramento.

The program will present the important features of Rural Health Council development. Subjects to be discussed are "The Physician and Rural Medical Care," "Public Health Service for the Rural Community," "Training of Registered Nurses and Nurses Aide Training," "Training of Physicians for Rural Practice," "Rural Health Care and the State Government," "Preventive Medicine for the Rural Child." In addition there will be discussions of the functioning of health councils, medical and hospital service plans, and rural hospital management and development.

INFORMATION

Physician-Patient Relationship with Regard to Automobile Accidents Under the California Financial Responsibility Law

PEART, BARATY AND HASSARD *of the California Bar*

In 1947 the California legislature passed what is commonly known as the *Financial Responsibility Law*. It was designed to make citizens of California safe against financially irresponsible drivers of motor vehicles. It declares that a motor vehicle operator who injures or kills another person, or damages his property in excess of $100.00, must be financially prepared to make a settlement with the injured party or his estate. If he fails to do so the operator must forthwith forfeit his privilege to drive a vehicle in California. The Act became effective July 1, 1948, and must be enforced by the Department of Motor Vehicles.

1. *Accident Reports Required:*

After July 1, 1948, the operator of every motor vehicle which is in any manner involved in an accident within California, in which any person is killed or injured or in which damage to the property of any person, including himself, in excess of $100.00 is sustained, *must report the matter in writing to the Division of Financial Responsibility, Department of Motor Vehicles, Sacramento, within ten (10) days.* If you are insured, you must still make the required report on a form provided by the Department of Motor Vehicles. This form is known as S.R-1. If you are not insured, then within sixty (60) days of filing the accident report you must meet the requirements of the Financial Responsibility Law, which include either depositing security in an amount deemed by the Department to be sufficient to meet any judgment for damages arising from the accident, or file with the Department evidence that you have been released from liability, or file with the Department a court judgment of non-liability or execute a confession of judgment payable when and in such installments as are agreed upon by both parties, or execute a duly acknowledged written agreement providing for payment of an agreed amount in installments. Failure to take one of these five steps will result in suspension of driver's license in California.

2. *Report on Persons Injured:*

S.R-1 is the official form used to report the accident or injuries to the Department of Motor Vehicles. A portion of the form is devoted to the report of the injuries and deaths caused by the accident. The act provides that the amount of security that will be required for deposit will be determined on the information made available to the Department. Therefore, the Department circular states that it is to the interest of the driver to give a complete explanation of the damage or injury to persons or property, and that he should furnish further proof of personal injuries in the form of doctor's reports and property damage in the form of correct estimates of repair costs, and that forms for this purpose are available.

3. *Physicians' Statements:*

To supplement S.R-1, the Department of Motor Vehicles has issued form S.R-5. This form, which calls for a physician's report on the nature, and extent of injuries, is to be used when the report form S.R-1 does not provide adequate space for fully describing the injury, or when more than two persons are injured, or in all cases of serious injury.

Both the Financial Responsibility Law and the forms state that any reports given in compliance with the Law are strictly confidential and cannot be used in court. The Law provides (Sec. 420.8 of the Vehicle Code) that:

"Neither the report * * * or the findings, if any, of the Department on which action is based, nor the security filed, as provided in this chapter, shall be referred to in any way or be in evidence of the negligence or due care of either party at the trial of any action at law to recover damages."

Form S.R-5 contains a section which is entitled, "Attending Physician's Report." In this section the attending physician is requested to:

1. Describe injuries resulting from the accident.
2. Probable period of disability.
3. All hospitalization.
4. Probable permanent injury or disfigurement.
5. Estimated amount of your total fee.
6. Estimated amount of other medical expenses.

Then there is a space for the signature of the attending physician and his address. Immediately below this there is a space containing the words, "I certify that the above report is true to the best of my knowledge." And under this there is a place for the signature of the injured person.

If the attending physician completes this form he immediately enters the field of privileged communications between physician and patient. One of the most important legal problems which may confront a physician in his relations with a patient are the rights, obligations and duties of the physician in connection with disclosure of communications which a patient may make to him. The privilege of non-disclosure is that of the patient and the physician cannot reveal facts which came to him from the patient as the result of the confidential relationship without the consent of the patient. There are, of course, several exceptions to this rule, and the entire subject has been

discussed in the April, May and June, 1946, issues of CALIFORNIA MEDICINE. The forms provided by the Department of Motor Vehicles, in an effort to meet the requirements of the Financial Responsibility Law, are not within one of the established exceptions to the rule and, therefore, if an attending physician completes Form S.R-5 and provides the Department of Motor Vehicles with any of the information which it requested therein, without first obtaining the consent of his patient, it is possible that the physician may be violating the confidential relationship existing between physician and patient.

It is, therefore, advised that physicians not fill out form S.R-5 unless the patient has expressly requested that such form be completed, and has evidenced this request by first signing the form himself.

The Proposed Plan of Action for Adequate Blood Coverage in the State of California

The people of the State of California must be supplied with the blood and blood derivatives essential to their medical needs in peace and war.

Every hospital in California should have adequate amounts of blood and blood derivatives available to meet the demands within that hospital.

Many counties of the state have inadequate blood coverage, or none at all. This is particularly true of our rural and mountain communities. Such inadequacy must, and will be corrected.

An overall plan of Blood Banks for the state is in order. A coordinated reciprocal system of blood banking between the various banks of the state is clearly indicated. The possibility of local disaster or any other untoward catastrophe points to the need for integration. One or more banks should supply a member bank if it is incapacitated, or if it is unable to provide sufficient blood or plasma for emergency needs.

Non-profit, community type blood banks have dramatically proven their value in peace and war to the community, to the state, and to the nation. Their number must increase. Many hospital blood banks are at present performing valuable service in smaller towns, but to have several such banks operating in a larger center is uneconomical in money, blood and technical personnel.

Regional blood banks will be encouraged and aided to expand their present facilities so that smaller adjacent towns can use their service. Local county medical societies, which serve those large sparsely settled areas of the state, will be asked to promote an active typing service on every adult. This so-called "walking blood bank" program has real value to the individual who is typed, and to the local physician who might require blood service assistance. We would specifically like to see Rh typing performed in conjunction with the blood typing. The reason for this recommendation is that we can provide a better method of protection to women when their Rh factor is known. Possible sensitization of an Rh negative woman by an Rh positive transfusion can be prevented if she has been previously typed. Laboratories in rural regions must be prepared to aid in this contemplated large scale typing program by seeing that their staff is technically equipped to perform the Rh studies.

The program of the Blood Bank Commission of the California Medical Association envisions the following:

1. To encourage, to promote, to sponsor, and to aid in the establishment of community type, non-profit Blood Banks in California wherever their establishment is clearly indicated. Control of such banks must be under the local county medical society.
2. To actively promote and strongly encourage high and uniform standards of service. The standards we recognize are those outlined in the Biologics Act of the U. S. Public Health Department.
3. To plan and foster a clearing house for questions relating to the training of personnel for blood banks.
4. To sponsor and aid local medical societies in developing "walking blood banks" in sparsely settled areas, where it is economically unsound to erect a blood bank. The Rh factor should be determined at the same time as the blood typing.
5. To promote and foster the immediate exchange of ideas, and materials, and the dissemination of information relating to blood banking, and its technical methodology by education publicity and research.
6. To plan and foster cooperation and integration of all existing and contemplated blood banks in time of emergency or disaster.
7. To aid other states and the nation, in regard to blood products, to the limit of our ability when disaster strikes, or when an emergency condition exists.

The Blood Bank Commission calls on every doctor in the state to actively interest himself in this proposed program. The scope of such a service is tremendous, its realization will require the enlightened and enthusiastic support of each one of us.

BOOK REVIEWS

PROGRESS IN CLINICAL MEDICINE. By Various Authors. Edited by Raymond Daley, M.A., M.D., Camb., M.E.C.P., and Henry G. Miller, M.D. Durh., M.R.C.P., D.P.M. With 22 text-figures and 15 plates. Grune & Stratton, New York, April 29, 1948. $6.00.

This book attempts to summarize recent progress in clinical medicine, and consists of 13 chapters by various British authors. It was of interest to the reviewer to note the contributions of British investigators. However, the emphasis on work from their own country, and consequent inattention to many significant contributions of American workers, has resulted in many instances in inadequate review of recent medical advances.

For example, the discussion of hepatitis makes no reference to the work of Cecil Watson, nor to the papers concerning inoculation in volunteers, and other related studies conducted during the war. There is an inadequate discussion of the use of penicillin in the treatment of subacute bacterial endocarditis, and of the importance of the "in vitro" sensitivity of the organism to penicillin, as well as the occasional importance of massive dosage. The whole of this subject is treated in only two pages, while the subject of peptic ulcer covers 15 pages. Here is an obvious imbalance in terms of the importance of the recent advances made in two fields. Again, only half of a page is devoted to the subject of surgery of pulmonary tenosis, despite the outstanding recent work in this problem. The chapter on renal diseases has no discussion at all of the present concepts of physiological disturbances in renal insufficiency and their rational management. Nor is any mention made of the use of streptomycin in urinary infections. The section on renal anoxia omits reference to the important fundamental work of Van Slyke and his associates, and to Lucke's significant paper. In fact, there is not a single reference in this section to American work, despite the important contributions made by investigators in this country.

Chapters which were of particular interest, however, were those on tropical medicine, by Frederick Murgatroyd, and on intestinal disorders, by F. Avery Jones.

The criticisms offered by the reviewer do not detract from the considerable amount of clinical information contained in this volume, which will benefit those seeking information on the major developments of the past decade. The emphasis on British work is understandable, and a similar fault might be found in such a composite work by American authors. This book can be read with profit by those unfamiliar with many of the important British contributions to clinical medicine in the past few years.

A HISTORY OF THE HEART AND THE CIRCULATION. By Fredrick A. Willius, M.D., M.S. in Med., Senior Consultant in Cardiology, Mayo Clinic; and Thomas J. Dry, M.A., M.S. in Med., Consultant, Section on Cardiology, Mayo Clinic. Illustrated. W. B. Saunders Company, Philadelphia and London. $8.00.

The authors preface their book by emphasizing the importance of the historical approach in the study of medicine. This position, undoubtedly sound, unfortunately has been too much neglected in this age when the rush of progress leaves little time for consideration of more than the exciting developments of the moment. Dr. Willius and Dr. Dry attempt to summarize the main currents of general history as they go along, but this is of course a difficult task in the amount of available space. The year 1453, for example, is mentioned as a boundary line between Mediaeval and Renaissance periods, but just what happened in that famous year is not stated. The book is well and interestingly written and is especially useful for the doctor because it summarizes events in chronological order as well as the lives of the important figures in cardiology. The biographies are brief, vivid and usable, and the sequential presentation of data according to subjects such as anatomy of the circulation, arrhythmias, congenital malformations, etc., is a real feature.

YOU AND YOUR DOCTOR. By Benjamin F. Miller, M.D., Clinical Professor of Medicine, George Washington Medical School. Whittlesey House, McGraw-Hill Book Company, Inc. 1948. $2.75.

This is a readable and extremely clever piece of propaganda in favor of the Wagner-Murray-Dingell Bill and similar plans.

The author paints a rosy picture of a theoretical state in which everyone would be well fed, well housed, well clothed, well educated and well cared for in a medical sense. He brusquely brushes aside Voluntary Health Insurance as of little value. His arguments will appeal to certain lay people who do not have the knowledge or perspective to evaluate them properly. If the author's plan were to be put into effect, it would require the establishment of an authoritarian state. He disregards completely the effect which this has had in other parts of the world and particularly its effect upon standards of medicine and medical care. He quotes certain statistics without adequate analysis and interpretation and on occasion uses the same argument to prove widely differing points.

It is the traditional Physician's Forum type of propaganda in new and attractive form.

SYNOPSIS OF PEDIATRICS. By John Zahorsky, A. B. M.D., F.A.C.P., Professor of Pediatrics and Director of the Department of Pediatrics, St. Louis University School of Medicine; assisted by T. S. Zahorsky, B.S., M.D., Senior Instructor in Pediatrics, St. Louis University School of Medicine. Fifth Edition with 158 Text illustrations and 9 Color Plates. The C. V. Mosby Company, 1948. $5.50.

This book was first written in 1934, primarily for medical students. It had 60 chapters which corresponded with 60 didactic lectures. Because a synopsis can never go into detail which is necessary and because of the magnitude of the field of Pediatrics, it falls short of its mark as a reference book for students and says too little about too large a number of topics. In this it shares a fault common to many synopses.

A readable personal style has been maintained and the book is liberally illustrated. It has an atmosphere and flavor which might be term "old-fashioned" as is illustrated in the index, where we find rachitis, cereal decoctions, dyspepsia, and eclampsis (convulsions) listed.

While the general practitioner may discover this book meets his requirements, it would appear that in most instances recent graduates would find a larger and more complete text came closer to doing so.

CLINICAL STUDIES IN PSYCHOPATHOLOGY — A Contribution to the Aetiology of Neurotic Illness. By Henry V. Dicks, M.A., M.D., F.R.C.P., Nuffield Professor of Psychiatry in the University of Leeds. Baltimore, The Williams and Wilkins Company, 1947.

The subject matter of this book stems from a series of postgraduate lectures given at the famous Tavistock Clinic in London. The contents presupposes a certain degree of familiarity with psychiatric jargon, particularly analytically oriented psychopathologic concepts, so that the volume is essentially directed at psychiatrists and other students of psychopathology who are primarily interested in the psychoneuroses, rather than at the internist and general medical man.

The author pertinently remarks that the recent war has turned what was considered the extravaganza of a small group on the periphery of "respectable medicine" into a much more widely accepted body of knowledge held valid by many in the social sciences and by many in the younger generation of physicians. However, another danger is arising with increasing acceptance—a lip-service reception of a total psychosomatic approach without foundation in deeper experience. Healthy changes appear to be happening to certain psychoanalytic concepts. Instead of an attitude of too rigid acceptance of older doctrine, analysts are broadening their conceptions of the variety of instinctive needs and drives in human personality, so that one hears increasingly about aggression, hostility, dependence, security, insecurity, anxiety, etc., instead of jamming every new experience into a pan-sexual theory. Certainly "fear of loss of love and security" is more easily comprehensible than the controversial "castration fear," for example.

Since the author adheres primarily to Freudian concepts, his therapeutic method utilizes free association, the interpretation of resistance, the examination of dreams, and the interpretation of the transference with particular emphasis on the tracing out of symptoms to their origin, at all times recognizing the emotional quality of the symptom.

The psychopathology of anxiety states, phobias, obsessional states, hysteria, sexual maladjustments, sexual perversions and drug addictions are taken up in turn. There are many case reports culled from the author's personal experience to exemplify his basic themes. In general, these are well chosen; if one does not always see clearly the reasons for a particular interpretation, this may be because the author is unable in a limited space to present all the facts.

In the final chapter three basic early biological needs of the human organism are described: a self-preservation tendency (infantile fear lies at the root of repression and emotional security is the essence of adjustment) a sexual tendency (Freud's libido), and aggressiveness. The mechanistic approach to human problems misses all that is essential, the author states. "The time is not now so far distant when the corpus of Medicine will once again achieve its own 'psychosomatic' unity. All around Medicine the social sciences are converging towards an integration under the primacy of psychodynamic concepts. Unless Medicine catches up with this movement it will find itself in a backwater, grappling with problems that bear but little relationship to the urgent needs of our time."

The psychoanalytically oriented physician will find much with which he can agree and sympathize here; the "constitutionally" oriented physician will consider much of the contents "wild flights of fancy," but whatever his theoretical prejudices, he will find the presentation sincere and stimulating.

SUBACUTE BACTERIAL ENDOCARDITIS. By Emanuel Libman, M.D., Late Consulting Physician, The Mount Sinai Hospital, New York City, and Charles K. Friedberg, M.D., Adjunct Physician, the Mount Sinai Hospital, New York City. Edited by Henry A. Christian, A.M., M.D., Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University. (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as in that work) Oxford University Press, New York, Second Edition, 1948. $3.50.

No one could be better fitted to write on subacute bacterial endocarditis than Dr. Libman, who grew up on the subject and contributed so much original work to the understanding of it. Being a textbook article, this little monograph is difficult to review. The subject is taken up systematically, and now, with Dr. Friedberg, is brought fully up to date so that the more recent spectacular developments of penicillin therapy are taken up in detail. There are numerous illustrations, a bibliography, and an index.

FOUNDATIONS OF NEUROPSYCHIATRY. By Stanley Cobb, A.B., M.D., fourth edition. Baltimore, The Williams & Wilkins Company, 1948. $2.50.

The fourth edition of this book shows very few important changes over the third edition. Certain parts dealing with cerebral blood flow, the types of neurons in the autonomic system and the motor areas of the cerebral cortex, have been largely rewritten.

The author clings to the term "neuropsychiatry," which many are now discarding. It is perhaps unimportant to quibble over this term, but as has been pointed out, the prefix "neuro" would make the term mean neurological psychiatry rather than neurology and psychiatry. The author's concept is that to understand both neurology and psychiatry, one must grasp certain fundamental anatomical and physiological facts about the central nervous system. This material is given in a very clear and distinct fashion and can be highly recommended.

The author then passes over to the "mind-body" problem and tries to clarify this difficult point. He argues for Jelliffe's concept of reversible and irreversible organic changes, rather than the concept of organic and functional as two different things.

The chapter on cerebral circulation is excellent and this is due, in part, to the author's own research work on this problem.

Neuropathology is next discussed, followed by a brief discussion of epilepsy. This takes four-fifths of the book and the other fifth is devoted to two chapters: "Some psychological concepts important in medicine" and "Psychopathology." The approach here is biological and, as far as it goes, there is a considerable amount of interesting material given.

In discussing psychopathology, the author states his preference for Meyer's concept of reaction types. He also follows Meyer in being a pluralist, and in trying to see in every case the various factors which bring about an abnormal reaction, rather than accepting the concept of a single precipitating factor.

The book can be recommended for general use by medical students. The biological basis of behavior is developed in as clear and simple a fashion as it is possible to do, and in highly controversial fields of schizophrenia and manic-depressive psychosis, the author quite properly insists on how little is known on the fundamental nature of these disorders, rather than giving a glib explanation, which might satisfy the student and lead him to think that these disorders really were understood.

Therefore, the book can be highly recommended for its purpose, which is to give the medical student some correlation between neuroanatomy, neurophysiology, and the general behavior of human beings.

PSYCHOLOGICAL ATLAS. By David Katz, University of Stockholm, with 400 illustrations. The Philosophical Library, New York.

This heterogeneous collection of illustrations, accompanied by brief explanatory notes, might conceivably be of value to the psychologist. Those illustrations falling within the field of interest of the reviewer are generally of poor quality; certainly better ones are available to anyone having access to a medical library. This compilation cannot be recommended to the physician.

INTERESTING AND USEFUL MEDICAL STATISTICS. Edited by William H. Kupper, M.D. Wm. C. Brown Company Publishers, Dubuque, Iowa. $6.50.

Unless one has a great appetite for tabular statistics *per se*, there is little of value in this book. It is a hodgepodge of unrelated tables on therapy, diagnosis, morbidity, mortality, lifted from their context, which destroys some of their value, and reprinted from various well-known texts and periodicals.

THE SKULL SINUSES AND MASTOIDS. A handbook of Roentgen diagnosis by Barton R. Young, M.D., professor of radiology, Temple University Medical School. The Year Book Publishers, Inc., Chicago, 1948. $6.50.

This is perhaps the best of the handbooks of roentgen diagnosis yet issued by the Yearbook Publishers. The illustrations are excellent. The text is sound and the propinquity of text and figure leaves nothing to be desired.

As in all handbooks, there are certain minor omissions, the importance of which is a matter of individual opinion. Under "congenital variations and disorders of the skull," fairly prominent place is given to such lesions as encephalocele and dermoid cyst which are comparative rarities, while mention is not made of the small cleft in the posterior portion of the parietal bone (which is so neatly illustrated in Sobotta's anatomy text) and which is not infrequently mistaken for fracture in roentgenograms of infants' skulls.

Some readers will question the wisdom of the use of the term "sinus*itis*" in the interpretation of roentgenograms of the nasal accessory sinuses. The radiologist can diagnose mucosal swelling or fluid, but cannot always distinguish between simple allergic swelling and true inflammatory disease.

One particularly satisfactory part of the book is the clear delineation of the technique used in various projections. This one feature alone makes the book valuable to every radiologist, as well as to most students and practitioners who have occasion to see roentgenograms of the skull.

VASCULAR DISEASES IN CLINICAL PRACTICE. By Irving Sherwood Wright, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College; The Year Book Publishers, Inc., Chicago, 1948. $7.50.

Without hesitation, this reviewer can state that Dr. Wright has performed an outstanding service in writing this monograph on vascular disease. The author has had wide personal experience in the diagnosis and treatment of patients with vascular conditions. In addition he has for many years been actively engaged in clinical research in the vascular field and has made numerous significant contributions. Many of these original observations are contained in this work. In this book, he has correlated the clinical findings with the underlying physiological and pathological processes. Furthermore, Dr. Wright has a wide background in general medicine, which enables him to evaluate vascular conditions in relation to the patient as an individual in modern society. Again and again he stresses the importance of "reviewing the patient as a whole rather than concentrating exclusively on the history and site of injury."

The first chapter is devoted to a classification of vascular diseases. The seven pages accorded to this subject indicate the variety of conditions embraced by this book and the importance of this subject in the medical curriculum. Then follows a splendid chapter on methods used in the study of the patient. The author emphasizes the use of simple clinical methods but amplifies their use with an excellent description of more complicated diagnostic procedures. With a nice appreciation of the relative importance of various clinical conditions, Dr. Wright then takes up obliterative vascular disease. The chapters on Arteriosclerosis and Buerger's Disease are outstanding. Details of treatment are excellently evaluated. The less common vascular diseases are briefly but clearly described, with illustrative case reports and good bibliographies at the end of each chapter. Diseases of the veins, thrombophlebitis, pulmonary embolism, and the technique of anticoagulant therapy are well described. Surgical procedures of use in the treatment of vascular disorders are briefly discussed in appropriate sections.

The book is nicely made up and bound, with liberal use of illustrations. The only adverse criticism is possibly the poor reproduction of certain x-ray films. The diagrams of blood vessels, both arteries and veins, although illustrative, are too complicated for clarity. There is an excellent index which permits the volume to be used easily for reference.

Above all, Dr. Wright has produced a readable book. Throughout, he has used a light touch; for instance, when he says, "to give a prognosis in any case of active thrombophlebitis is hazardous—especially to the reputation of a physician prone to this form of mental gambling." But he does not hesitate to stand firm on principles. For instance, in speaking of the use of anticoagulants in the prevention of thrombosis encountered in patients with polycythemia, he states: "In some, anticoagulant treatment was exceedingly difficult. However, because it may be life-saving, the risks must be taken and the physician should be willing to assume the responsibility in order to preserve the patient's health and even his life."

Dr. Wright's monograph is a classic. What Kanavel did for surgery of the hand and Sir Thomas Lewis did for our understanding of heart disease, Wright has done for vascular diseases. This book is recommended without reservation and alike to medical students, to those interested in circulatory disorders, and to all physicians.

LABORATORY DIAGNOSIS OF PROTOZOAN DISEASES. By Charles Franklin Craig, M.D., M.A., Colonel, United States Army Medical Corps (retired), D.S.M. Emeritus professor of tropical medicine, Medical School, Tulane University. Second edition, 56 illustrations and 7 colored plates. Lea & Febiger, Philadelphia, 1948.

Colonel Craig's Laboratory Diagnosis of Protozoan Diseases now appears in a second edition made necessary by the additional data documented since 1942 and by exhaustion of the first edition. The new edition is enlarged by 35 pages, two illustrations, and three colored plates. It thoroughly reviews advances of the last six years and retains the author's masterly and highly authoritative judgments on practical methods of diagnosis. It includes detailed descriptions in terms of medical use of amebas and flagellates, leishmanias, trypanosomes, coccidias, malarial plasmodia and balantidium.

It is distinctly supererogatory to criticize details in a text such as this. A few points only are deserving even of mention and these in no wise detract from the excellent quality of the book. In the diagnosis of amebiasis there are some workers who do not believe that the motile trophozoite (unstained) can be safely identified in the average case by the average technician or physician. There is a difference of opinion as to the value of learning the detailed morphology of intestinal protozoa other than *E. histolytica.* This applies very strongly to the effort to teach such detailed morphology to medical students and physicians. Under the diagnosis of kala azar by gland puncture, it is not noted that superficial gland enlargements are common in patients in North China and are apt to be absent in other geographic areas. The work on pre- or exo-erythrocytic forms of malarial plasmodia, especially that during the last two years, might receive more intensive description; and the practical diagnostic importance of examination of living (unstained) plasmodia is perhaps exaggerated.

One of the most valuable features is the Critique of Diagnostic Methods in each section. This puts at the reader's disposal the ripe judgment of the author on the selection and interpretation of methods. These sections are characterized by balance, restraint, undeviating adherence to practicality and they summarize the subject superbly.

The volume itself has the advantage, particularly for a laboratory manual, of lying flat when opened. The typography and proofreading are in keeping with the standards of perfection that we have come to associate with all of the author's publications. The indexing is fully adequate and accurate. The author can be congratulated on this thoroughly excellent text. It is a "must" for every laboratory of clinical medicine, either private or public.

TUBERCULOSIS, A Discussion of Phthisiogenesis, immunology, Pathology, Physiology, Diagnosis and Treatment. By Francis Marion Pottenger, A.M., M.D., Ll.D., F.A.C.P. Emeritus professor of medicine, University of Southern California, medical director of the Pottenger Sanatorium and Clinic for Diseases of the Chest, Monrovia, California. Price $10.00. Pages 597, with 105 illustrations and charts. The C. V. Mosby Co., St. Louis 3, 1948.

This book is well printed, accurately proofread, on good paper and satisfactorily bound. Though called "Tuberculosis" it deals almost exclusively with pulmonary tuberculosis. Here is the epitome of fifty years' study by one of the outstanding clinicians of our times. The tone of the book is set in the preface. "In these pages I shall frequently question accepted ideas, and in the development of my subject I shall attempt to give the facts, and when the truth is not clear I hope my presentation will be guided by logical discussion.... We have arrived at the place where every one of our theories must be subjected to careful scrutiny. . . . I have found I can work best when I can give a reason either for believing a certain thing or for following a certain course; or when I can say to myself positively that I do not know."

The author believes that tuberculosis is a relatively mildly infectious disease, often healing spontaneously. The case for the endogenous source of the bacilli in producing clinical tuberculosis is well presented, almost convincingly. The explanation of why the apex is most commonly invaded is excellently done, with special emphasis on the newer work of Cournand showing that the apex is practically anemic when the body is erect. Physical diagnosis is emphasized, particularly inspection and palpation. Many will applaud his belief in the limited values of auscultation.

The basis of all treatment is rest, flat in bed, the pulmonary apex level with the heart, adequate diet, agreeable surroundings and peace of mind. Surgical procedures are not needed as often as they are employed, but do have a definite place although as a wag put it recently "not to the point of bilateral pulmonectomy." The fact that pneumothorax is often a means of keeping control over a patient should not bind us to the realization it would be frequently unnecessary if the patient would stay in bed long enough. A good argument is advanced for the therapeutic use of tuberculin which probably will meet opposition. However, the reader should hear the author out to the end.

The captious critic may always find much to argue about. However, these comments appear justified: On pages 192, 334, 472 and elsewhere the author seems to assume there is fermentation and formation of gas in the stomach. On page 302 the patch test is called unreliable. In presenting almost every case, the author elicits an antecedent history of "influenza." Most of us, except in epidemics, use this word to cover a vague syndrome of fever, malaise and variable pain. It is more scientific to suppose these prodromal symptoms are actually due to the known existing tuberculous infection rather than the convenient catch-all "influenza." Many will wonder why strychnia and digitalis are mentioned for long continuing pulmonary hemorrhage and no word is said of transfusion.

There is much repetition, possibly unavoidable in textbooks, and the book could be used less strenuously if the illustrations and charts were turned upright so that constant shifting was unnecessary. But in general it is excellent. The open-minded, non-dogmatic approach to each problem, the frequent avowals of complete ignorance, the candid declarations that the author is guessing, the cold disdain of many medical "truths," all warm the cockles of a skeptical heart. Here is no doddering senile, but the agile mind of a brilliant scholar far below his chronological age. A hundred years from now, when tuberculosis is unknown in this country, this may well be the one book medical scholars will study to recapture the mature judgment of our day that led to the abolition of the white plague.

TEXTBOOK OF PUBLIC HEALTH (Formerly Hope and Stallybrass). By W. M. Frazer, M.D., Barrister-at-Law, Gray's Inn Medical Officer of Health, City and Port of Liverpool; and C. O. Stallybrass, M.D. (State Medicine), Deputy Medical Officer of Health, City and Port of Liverpool. Twelfth Edition. The Williams and Wilkins Company, 1948. $6.50.

This book is one of the most successful texts written for the public health workers of Great Britain. It incorporates in the presentation of the principles of public health all relevant British legislation. Besides purely environmental problems and those of control of communicable disease, the book includes the important aspects of maternal and child hygiene, school medical service, genetics, mental hygiene, welfare of the blind, hospital administration and social services. The latter two subjects in particular have been extended very greatly by the recent legislation of the Labor government and the authors have taken great pains to bring their text completely up-to-date in those matters.

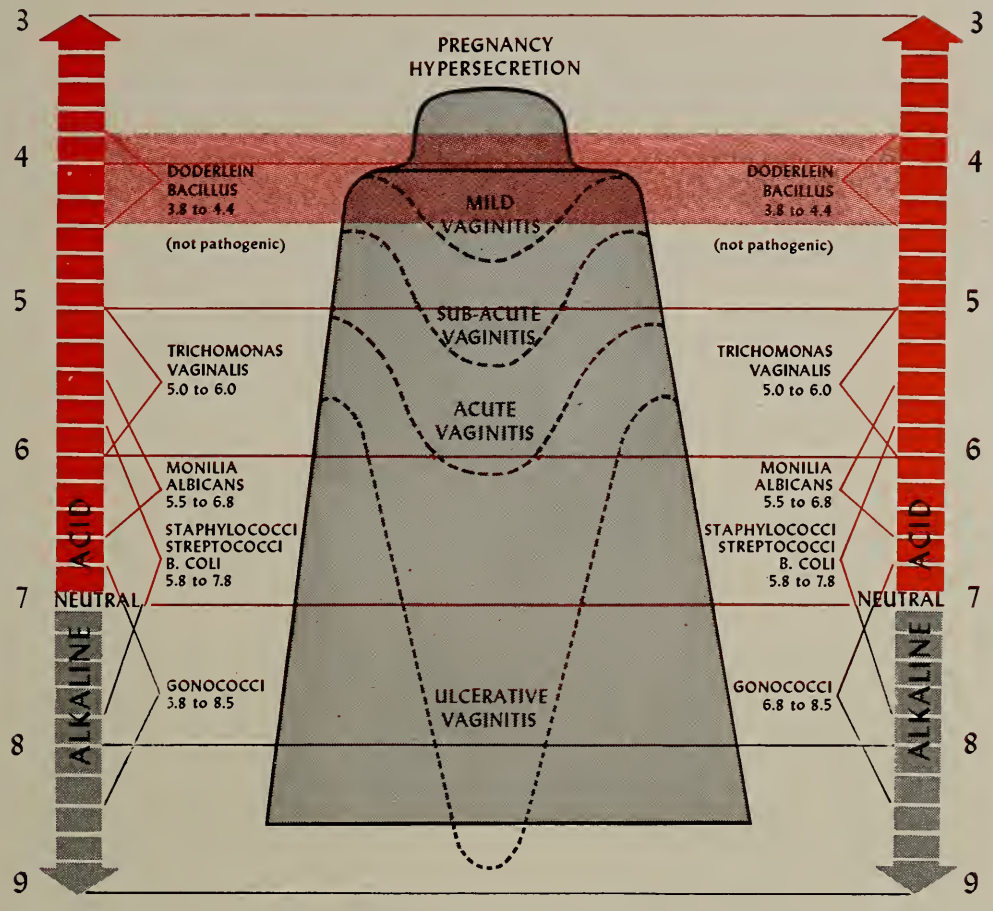
The book could serve as a useful reference volume for one wishing to compare British and American practices. Thus from it the American professional public health worker may glean useful ideas. However, it is focused so strongly on British procedures that the American medical student or practitioner would use it infrequently. Furthermore, even in the generally admirable chapters on epidemiology and infective diseases for which Stallybrass is world-famous, one seeks in vain for mention of residual DDT spraying, active immunization against tetanus or the congenital sequelae of rubella in early pregnancy, to mention three widely divergent subjects. While indispensable for the British Medical Officers of Health, C.P.H. and D.P.H. students, its main place in America would be in medical libraries and in libraries of larger health departments.

A TEXTBOOK OF BACTERIOLOGY. By R. W. Fairbrother, M.D., D.Sc. (Man.), F. R. C. P. (Lond.), Director of the department of clinical pathology, Manchester Royal Infirmary; special lecturer in bacteriology, University of Manchester; late deputy director of pathology, 21st Army Group (Col., R. A. M. C.). Fifth edition, 1948, 480 pages with 5 plates and 13 illustrations. Fabricoid. Grune & Stratton, Inc., 381 Fourth Avenue, New York City 16. Price $6.00.

The present edition of the excellent and well-organized textbook takes cognizance of some of the newer knowledge of bacteriology accumulated during the war. As a condensation it will again be welcomed by students of both biology and medicine, since the essentials are succinctly summarized in the tables and a few illustrations. Unfortunately, Plates I, II and III are so schematic that they give but a fleeting and not absolutely correct impression. Plate IV in particular is quite unsatisfactory. The critical American reader will doubtless find minor inaccuracies and significant omissions. For example, in Chapter XX, nothing is said regarding the high therapeutic value of the sulfonamides in bubonic plague. On page 363 it is stated that the "spores of *Cl. botulinum* are relatively resistant to the action of heat." Although for the majority of European strains of *Clostridium botulinum* this statement is correct, as far as it applies to American strains it is a definite understatement. Even in a short textbook it is advisable to express spore resistance in a time-temperature equation. Notwithstanding these inadequacies, the book will prove valuable as an introduction to a course in bacteriology.

DIABETES MELLITUS IN GENERAL PRACTICE. By Arthur R. Colwell, M.D., associate professor of medicine and director of medical specialty, Northwestern University Medical School. The Year Book Publishers, Inc. $5.25.

This is a poorly written book which fails utterly in its purpose of clarifying the treatment of diabetes to the average practitioner.



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FEVER THERAPY MAKES PENICILLIN MORE USEFUL AGAINST SYPHILIS

Artificially produced fever increases the effectiveness of the seven and a half day penicillin treatment for syphilis to more than 80 per cent, a substantial improvement over both penicillin alone and penicillin and mapharsen in combination for the same length of time.

This valuable use of fever therapy is described by Herman N. Bundesen, M.D., president of the Chicago Board of Health, and a group of four doctors who assisted him, in an article which appears in a recent issue of *The Journal of the American Medical Association.*

Three of the doctors—George X. Schwemlein, research associate at the Kettering Foundation for Medical Research, Cincinnati, Ohio; Theodore J. Bauer, senior surgeon of the United States Public Health Service and venereal disease control officer, Chicago, Ill.; and Robert M. Craig of Dayton, Ohio —together with Dr. Bundesen, pioneered the penicillin and penicillin-mapharsen treatments for syphilis.

In comparison with the 80 per cent effectiveness of penicillin and fever therapy in seven and one-half days their tests show penicillin 70 per cent effective and penicillin given with mapharsen, a compound of arsenic, 49 per cent effective against syphilis in seven and one-half days.

The fourth physician in the research group is Jack Rodriquez, medical director of the Chicago Intensive Treatment Center, Chicago, Ill., where the group tested the fever and penicillin method from January 4 through July 29, 1945.

Each patient was given an injection of sodium penicillin every three hours for 60 doses, plus three 3 hour sessions of artificial fever on alternate days, begininng 23 hours after the penicillin was started.

Fever therapy, however, does not cut down the time required for penicillin treatment, the doctors found. When they gave patients the same amount of penicillin—1,200,000 units—in about 30 hours and reduced the fever therapy to one six-hour session, the treatment was effective in only about 60 per cent.

Neither is giving large amounts of penicillin without fever therapy more effective, the article indicates, citing research not yet completed. When patients were given 25,000,000 units of penicillin in 24 hours during this research, the drug was about 65 per cent effective.

In all, the doctors treated 120 patients under the penicillin-fever method, including 64 who were in the secondary stage of syphilis and nine whose blood tests did not show the disease. Eleven of the group did not finish treatment—eight because of lack of cooperation with the doctors, two because of cardiovascular fatigue during the period of fever therapy, and one because of uncontrollable fever. All syphilitic lesions healed immediately after treatment, although no more quickly than with penicillin alone, the doctors comment.

No serious reactions were noticed by the doctors. Sixty-four of the 100 patients whose blood tests were

(Continued on Page 38)

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PROTEIN THERAPY UNSUCCESSFUL FOR PEPTIC ULCER, SAY DOCTORS

Protein hydrolysate, predigested protein, is of little value in treating peptic ulcer, five Cleveland, Ohio, doctors report.

Writing in a recent issue of *The Journal of the American Medical Association*, the doctors—Edward E. Woldman, David Fishman, Richard S. Knowlton, A. Ashley Rousuck, and Willard C. Stoner—describe their findings from a study made at the department of gastroenterology, St. Luke's Hospital, Cleveland.

Protein hydrolysate therapy, also known as amino acid diet because the protein is made up of amino acids, is one of the comparatively new treatments for peptic ulcer and one which has been regarded as extremely promising.

Developed by Dr. Frank Co Tui of the New York University College of Medicine and the New York University Division of Surgery, Bellevue Hospital, New York City, and his associates, it consists of regular feedings of protein hydrolysate and carbohydrates for a period of two or three weeks. Supplementary vitamins are also given.

Many of Dr. Co Tui's patients were relieved of pain within 24 hours after the treatment was begun. Even in "intractable" cases—those who had not improved on complete bed rest and strict Sippy treatment—the ulcers became inactive. The alkaline Sippy powders neutralize excess acidity in the stomach and, combined with a mild, soothing diet, have long been used for treating peptic ulcer.

Dr. Co Tui's theory was that the high caloric and high protein diet rehabilitated the strength and body weight of the ulcer patient as well as prevented overacidity in the stomach. Many peptic ulcer patients, he found, were deficient in protein.

Such protein deficiency is brought about by an unbalanced choice of foods rather than by the ulcer patient's inability to retain or digest proteins in ordinary forms, the Cleveland study indicates. None of the 22 peptic ulcer patients treated in the study showed protein deficiency.

To test the therapy, the doctors administered a continuous drip of 10 per cent protein hydrolysate for 14 days through a tube inserted into the patient's stomach through the nose.

Although protein hydrolysate lowers the free acidity as long as the preparation remains in the stomach, they found that its after effect is to raise the patient's stomach acidity to a higher level than it was before treatment.

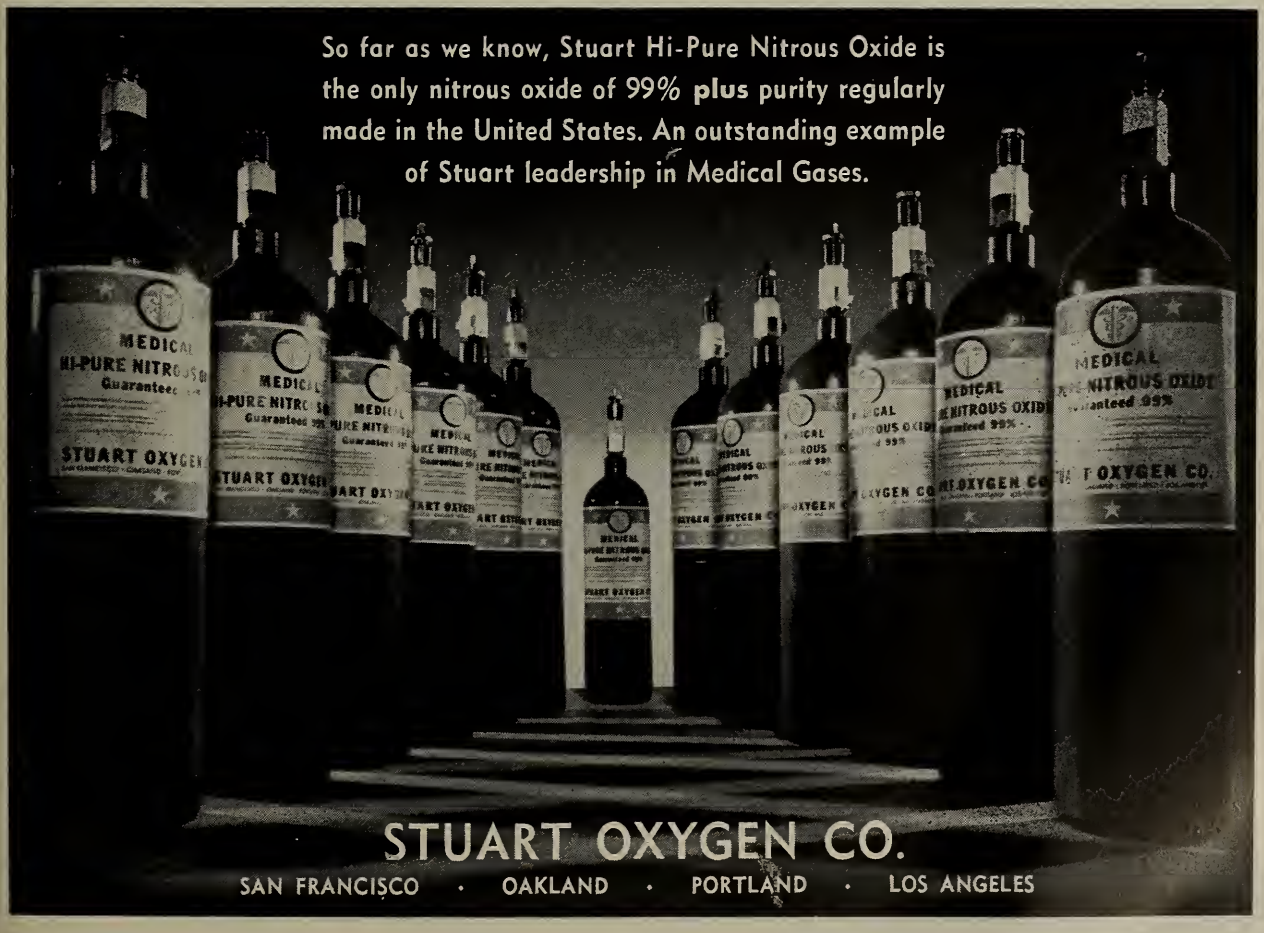
"When protein hydrolysate leaves the stomach," they say, "there is apparently a stimulation of the production of more free acid to a higher level than the original state.

"The presence of the amino acids in the upper part of the small intestine apparently causes a hormone to be liberated which stimulates the secretion of hydrochloric acid."

Protein hydrolysate also ceases to counteract stomach acidity after being given in repeated small doses, they explain.

In most of the 22 patients, free hydrochloric acid was observed in the stomach despite the continuous

(Continued on Page 38)



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FEVER THERAPY MAKES PENICILLIN MORE USEFUL AGAINST SYPHILIS

(Continued from Page 34)

positive for syphilis achieved negative blood tests. In 16 of the 109 patients who completed the seven and a half days, the treatment failed—that is, their blood tests were considered significantly positive by the doctors.

Two of these 16 had relapses of primary syphilis and five had relapses of secondary syphilis. In five the primary stage of the disease progressed to the secondary, and four who had achieved negative blood tests again had positive ones 12 months afterward.

PROTEIN THERAPY UNSUCCESSFUL FOR PEPTIC ULCER, SAY DOCTORS

(Continued from Page 35)

drip of protein hydrolysate. Ulcer pain continued for 24 to 72 hours, and in some patients the pain recurred later during the treatment. A month after treatment was discontinued, eight patients had ulcer symptoms again.

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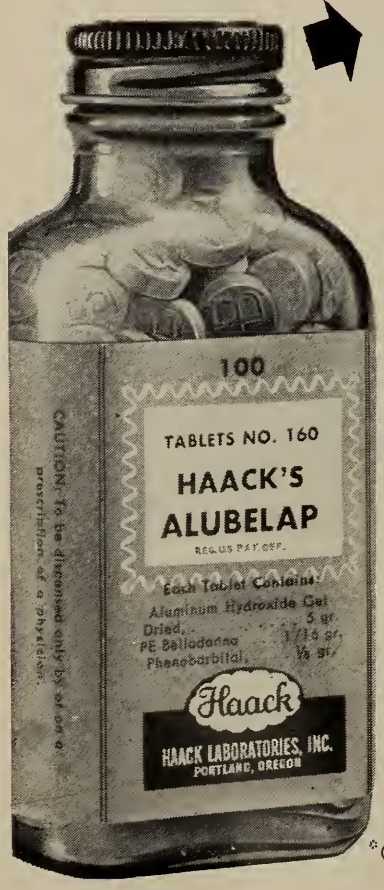
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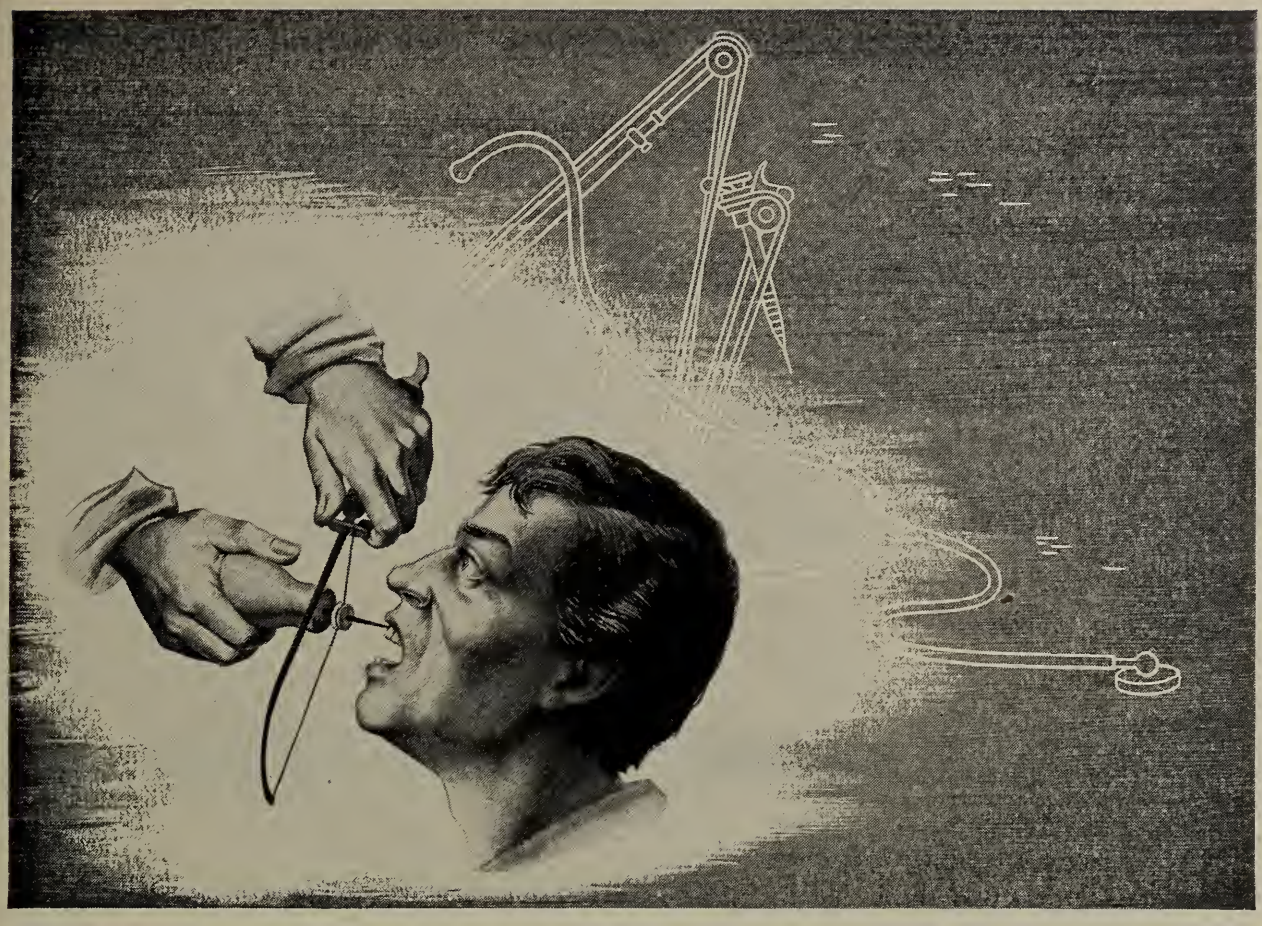
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In 1826 Leonard Koecker's scholarly *Principles of Dental Surgery* presaged the demise of practicing laymen—a prophecy that ripened with the founding of the first dental college at Baltimore in 1840. Chapin A. Harris' *American Journal of Dental Science*, published in 1849, heralded the coming of other early educational and fraternal magazines, some of which still serve the profession today.

★ ★ ★

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SECRETARY OF COUNCIL ON EMERGENCY MEDICAL SERVICE

Dr. Harold R. Hennessy has been appointed to the newly-created office of Secretary of the Council on National Emergency Medical Service of the American Medical Association. Dr. James C. Sargent, Milwaukee, Wis., is chairman of the council, which was formed in 1947 to coordinate medical efforts associated with a national emergency.

Dr. Hennessy has been associated with the A.M.A. Council on Industrial Health since February, 1946.

Dr. Hennessy, who received his M.D. degree from the University of Minnesota, held various assignments during the war years, his last being that of head of the Public Health Section in the Office of the Surgeon, Fifteenth U. S. Army. He received several military decorations, including the Order of Orange-Nassau Degree of Office With Swords from the Netherlands government.

PHYSICIANS NUMBER 199,755, A.M.A. BUREAU FINDS

The Bureau of Medical Economic Research of the American Medical Association estimates that there were 199,755 physicians in the United States as of June 1, 1948.

Frank G. Dickinson, Ph.D., director of the Bureau, says in an article which appears in a recent issue of *The Journal of the American Medical Association*, that this number is 17 per cent greater than the 170,163 physicians shown in the 1940 A. M. A. Directory. The population of the United States has increased only 12 per cent since 1940, he points out.

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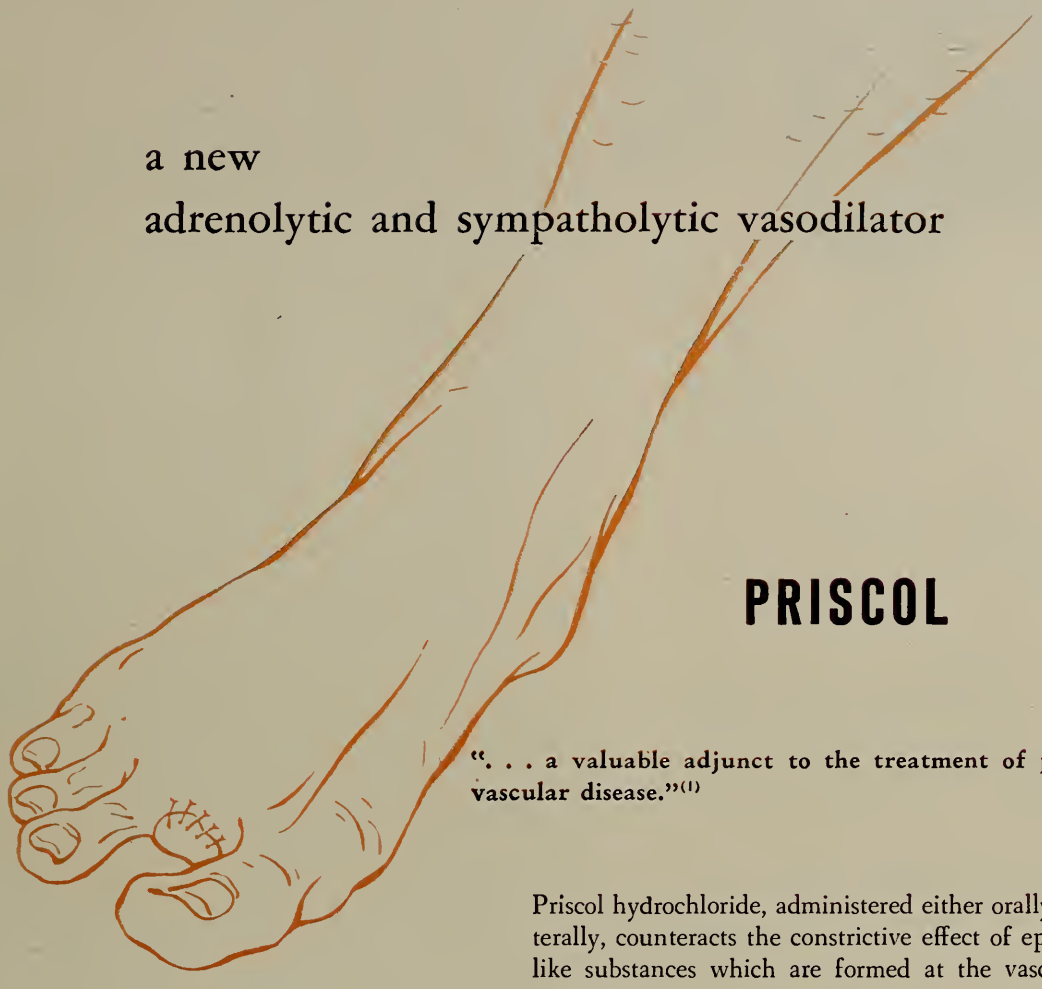
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1. Grimson, K. S., Marzoni, F. A., Reardon, M. J., and Hendrix, J. P.: *Surg.*, 23:728, 1948.

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1. Kasper, J. A. and Jeffrey, I. A.: A Simplified Benedict Test for Glycosuria, Amer. J. Clin. Pathology, *14*:117-21 (Nov.) 1944.

2. Haid, W. H.: The Use of Screening Tests in the Clinical Laboratory, J. Amer. Med. Tech., *8*:606-14 (Sept.) 1947.

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MEDICAL SCHOOLS NEED INCREASED FINANCIAL SUPPORT

The need for additional financial support is one of the most important problems confronting medical schools, the American Medical Association announced recently.

This need is pointed out in the 48th annual report on medical education in the United States and Canada by the Council on Medical Education and Hospitals of the American Medical Association. The report is published in a recent issue of *The Journal of the American Medical Association.*

Donald G. Anderson, M.D., Chicago, secretary of the council, who prepared the report with the assistance of Miss Anne Tipner, states that for the school years 1948-1949 the budgets of the medical schools and basic medical science schools in the United States total $51,000,000, an increase of $8,000,000 over the total for the years 1947-1948.

These schools owe much of their success in meeting the problems of inflation to the loyalty of their staffs, whose salaries in many cases have not kept pace with the rising cost of living, the report states. However, the problems presented by inflation and the recognition that advances in medical education could be made if more funds were available are causing those who are responsible for the conduct of medical education concern as to whether satisfactory progress can be maintained in the future.

Medical schools in the United States are at present admitting the maximum number of students that their facilities will permit without lowering educational standards, Dr. Anderson states in the report. The total enrollment, excluding students taking a required intern year, in the 70 medical and seven basic medical science schools in the United States during the academic year 1947-1948 was 22,739 students.

Although this figure is 1,161 less than the total enrollment for 1946-1947 if the extra classes that were in session during that period as carry-overs from the war-time accelerated program are included, a number of schools are accepting more students than can satisfactorily be accommodated, he points out. The enrollment of 22,739 students is 1,212 greater than the average enrollment during the five-year period, 1937-1941, immediately preceding World War II.

Had the junior class of 1947-48 been at full strength when admitted, the enrollment in the medical schools would now exceed 23,000, the report states. This group entered medical school in the academic year 1945-1946 as the smallest freshman class in the past seven years. At the time this class was selected, there was no provision for the deferment of premedical students by Selective Service.

In editorials which appeared in a recent issue, *The Journal* comments:

"The need for additional financial support to stabilize their present programs and to undertake essential new developments continues to be one of the most important problems facing the medical schools. While medical schools have been forced to increase tuition fees in recent years, student fees will still provide only 25 per cent of the cost of operating the medical schools in 1948-1949. The high quality of medical education in the United States has been made

possible only by the support which medical schools have received through endowments, gifts, university funds, and state and municipal tax sources.

"Sixty-six of the 70 approved medical schools in the United States have stated that they cannot admit more students with their present facilities for instruction in the preclinical departments. Thirty-seven of these schools have indicated that to admit more students an expansion of their clinical facilities would also be necessary, as have the four schools that did not report a need for additional preclinical facilities.

"Expansion requires much more than providing additional classroom space. Additions to laboratories and hospitals and the expansion of libraries, administrative offices, and other central departments would also be necessary. It should be clear from the council's report that the problem of increasing enrollments is not simple and that no school is likely to undertake to expand its facilities unless the need is unmistakably clear and sufficient financial support to meet the expense is assured."

The national headquarters of the Selective Service System has conferred with representatives of the medical schools concerning policies whereby a certain number of students in premedical courses will be given consideration for deferment, the report states.

These policies are expected to be published shortly in a directive for the Selective Service System, although they may not be forthcoming until the local boards are completely established.

In another editorial which appeared in the same issue, *The Journal* states:

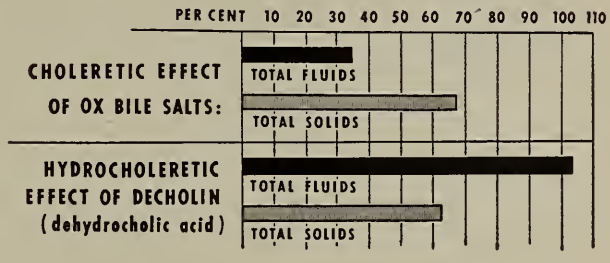
"The Selective Service Act of 1948 renders liable for service in the armed forces men between 19 and 25 years of age, the age group from which the great majority of premedical and medical students are drawn. There does not seem to be any question that the deferment of medical students and physicians in their first year of internship will be authorized. Selective Service officials have indicated that they recognize the importance of allowing a sufficient number of students to continue their premedical education so that the number of students and graduates will not be reduced in the years ahead.

"It seems probable that satisfactory provisions will be made for deferring an adequate number of premedical students. The importance of such a provision cannot be overestimated. The present Selective Service Act affects students who would, in the normal course of events, be entering medical school as late as the fall of 1953. Its effect on the production of physicians may thus be felt as far in the future as 1957. While veterans and others not liable for military service under the Selective Service Act now comprise a high proportion of the students in medical schools, during the next several years the schools will have to draw more and more of their students from the group liable for military service.

"During the latter years of World War II no provision was made for deferring premedical students. A decrease in enrollments occurred that was kept from progressing to serious proportions only by the unexpectedly early termination of the war. In the interest of the nation's health and safety, the possi-

(Continued on Page 48)

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Ivy, A. C., et al: Am. J. Dig. Dis. 7:333 (Aug.) 1940.

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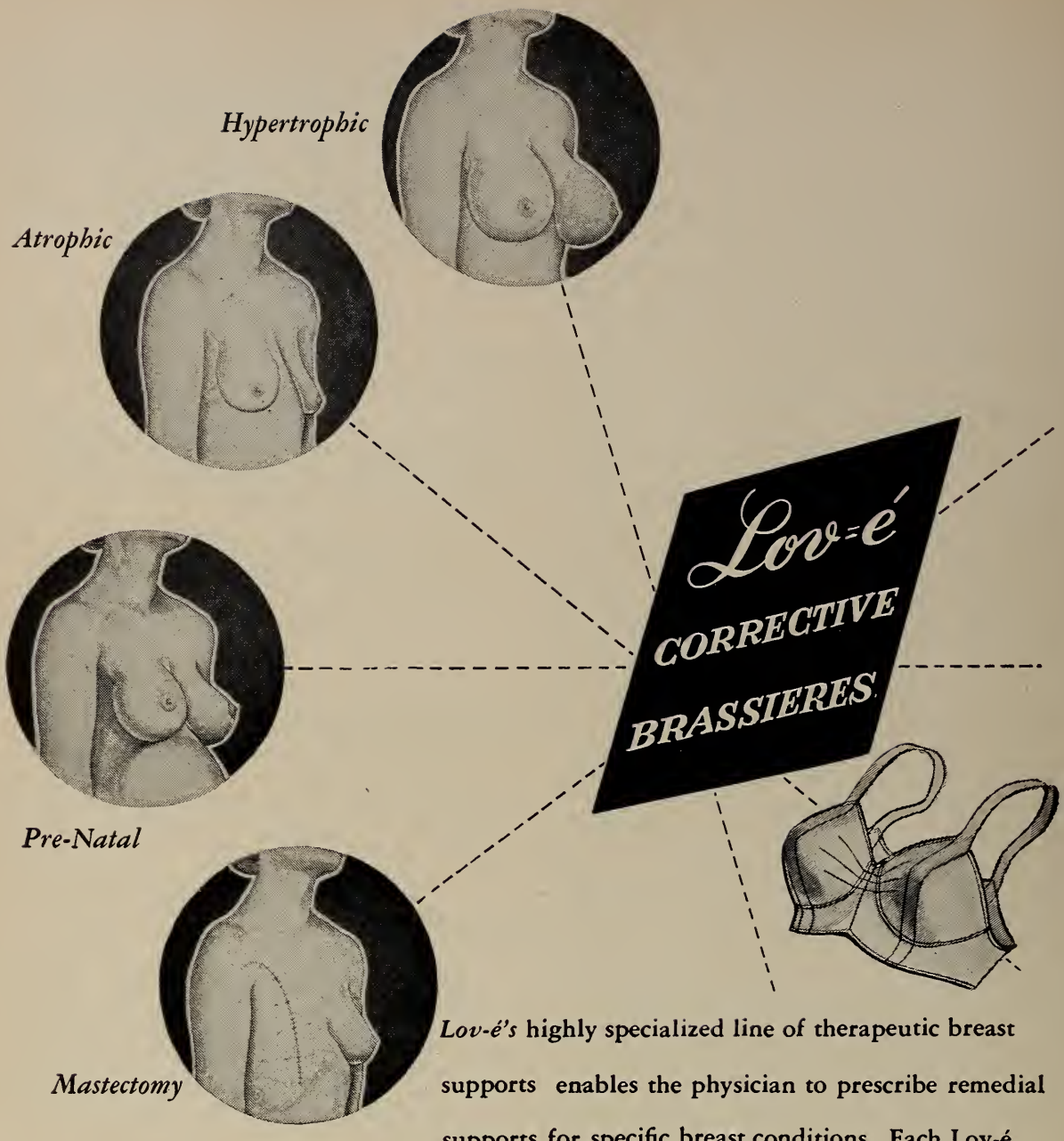
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MEDICAL SCHOOLS NEED INCREASED FINANCIAL SUPPORT

(Continued from Page 48)

in 1946-1947. Preliminary estimates of the composition of the 1948 freshman class indicate that about 68 per cent of the students will be veterans, *The Journal* states in an editorial which appears in the September 4 issue. The total enrollment of veterans in the medical schools and schools of the basic medical sciences in the United States increased from 55.6 per cent in 1946-1947 to 60.9 in 1947-1948.

Women comprised 9.5 per cent of all medical students in the United States during 1947-1948. This is the highest proportion of women students ever recorded. However, the percentage of women in the freshman class declined from 11.1 per cent in the preceding year to 7.9 per cent.

The total recorded attendance at refresher and continuation courses for physicians was 82,803. This figure, which does not include the attendance at 114 courses for which no attendance records were submitted, represents more than 40 per cent of the total number of living physicians in the United States.

There were 447 students in the required intern year in the United States. The medical schools and schools of the basic medical sciences in the United States estimate that they will enroll 6,407 freshman students during the academic year 1948-1949.

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PATIENT ADMITTED TO HOSPITAL EVERY TWO SECONDS LAST YEAR

During 1947 one patient was admitted to a hospital in the continental United States every two seconds and a live baby was born in a hospital every 11 seconds, according to the 27th annual report of the Council on Medical Education and Hospitals of the American Medical Association.

Four physicians—F. H. Arestad, E. H. Leveroos, W. R. Albus, and W. W. Corbett—present the council report in a recent issue of *The Journal of the American Medical Association.* Their figures reveal that in comparison with 1946 the number of hospital beds has decreased from 1,468,714 to 1,425,222 and the number of admissions has increased from 15,153,452 to 15,829,514.

This apparent discrepancy is clarified when the average length of stay per patient in general hospitals is considered. In 1946 the average patient remained 12.9 days in a general hospital; in 1947 he was discharged after 11.4 days, a gain to the patient of a day and a half. The number of patient days has decreased from 452,400,710 to 444,288,585.

Represented in the report are 6,276 hospitals registered by the American Medical Association, including 1,909 approved for internships and residencies and 2,609 accredited by the American College of Surgeons as meeting unconditionally its minimum requirements for general standardization. The number of hospitals is four less than reported in 1946.

The decrease in total bed capacity is accounted for entirely in the government group of hospitals, federal hospitals alone reporting 51,282 beds less than last year. With admission to the government hospitals decreasing by nearly 394,000, admissions to civilian hospitals increased by more than 1,000,000 for the second consecutive year.

Births reported passed the two million mark (2,136,373) for the first time in 1946; during 1947 births in registered hospitals reached the still higher figure of 2,837,139.

Of every 1,000 patients entering these hospitals

(Continued on Page 56)

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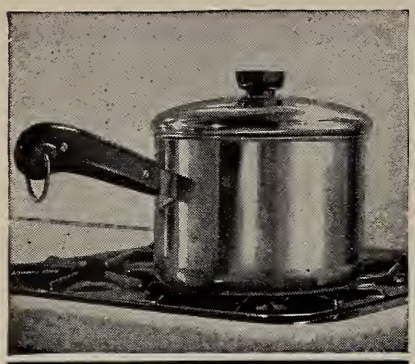
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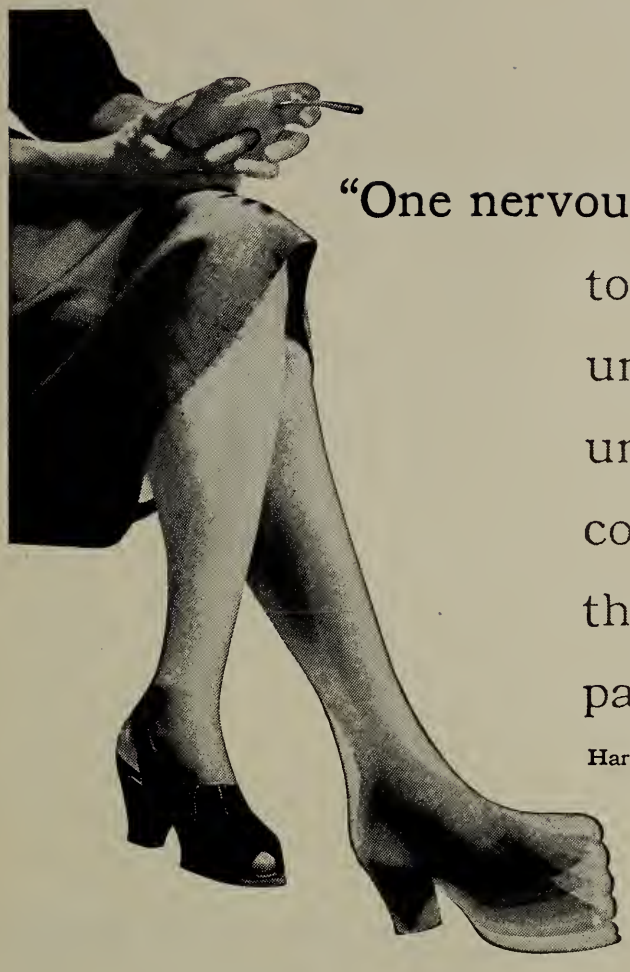
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PATIENT ADMITTED TO HOSPITAL EVERY TWO SECONDS LAST YEAR

(Continued from Page 51)

during 1947, 926 were admitted to general hospitals, 18 entered neuropsychiatric institutions, 14 were admitted to related institutions including convalescent homes, ten to isolation units, seven to eye, ear, nose and throat, six to tuberculosis sanatoriums, six to maternity hospitals, six to children's, four to industrial, and three to orthopedic hospitals.

There were 15,829,514 admissions exclusive of outpatients and newborn infants in all registered hospitals during 1947. For comparison it may be noted that in the period 1933 to 1945 the hospital admissions increased from 7,037,982 to 16,257,402. The greatest annual gain, a total of 2,829,088, occurred in 1943, with subsequent increases of 662,150 in 1944 and 220,554 in 1945. This trend was sharply reversed in 1946 when the number of admissions decreased by 1,103,950; however, 1947 shows an increase of 676,062 admissions.

The government hospitals with 72.3 per cent of the bed capacity reported 4,204,344 admissions or 26.5 per cent of all patients admitted in 1947. The non-government hospitals with 27.7 per cent of the beds had 11,625,170 admissions, or 73.5 per cent. The corresponding ratios in 1946 were 33 and 67 per cent.

The general hospitals continue to offer a tremendous volume of hospital service, as evidenced by the report of 14,665,195 admissions in 1947, or 92.7 per cent of all patients admitted.

The mental hospitals with a total of 680,913 beds had 291,954 admissions, or 1.8 per cent of all patients admitted in 1947. In comparison with last year there was an increase of 20,745 admissions with gains reported in all government and non-government classifications.

Tuberculosis hospitalization remains about the same with a total of 99,080 admissions in the tuberculosis sanatoriums as compared with 99,741 in 1946.

The enormous volume of service rendered by hospitals in the United States is likewise reflected in the daily patient load, which averaged 1,217,229 in 1947, exclusive of newborn infants. Compared with 1946, the daily census shows a decrease of 22,225.

The occupancy rate for the general hospital group to which 92 per cent of all patients were admitted decreased from 77.4 per cent in 1946 to 77.1 per cent in 1947. The percentage of beds occupied in government hospitals shows an increase in 1947 for all groups except the hospitals operating under federal control. The percentage of beds occupied in nervous and mental hospitals increased from 94.2 in 1946 to 95.7 in 1947 and nervous and mental diseases still account for more than half of the patients occupying hospital beds. Of the average census of 1,217,229 patients, 53.5 per cent were in hospitals of this type.

Registered hospitals reported employing 167,354 graduate nurses exclusive of 30,996 private duty nurses during 1947. The corresponding figures for 1946 were 146,602 and 28,245.

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References: 1. Gold, Harry: In Conferences on Therapy, N. Y. State J. of Med., Mar. 1, 1947. 2. Goodman, L. and Gilman, A.: The Pharmacological Basis of Therapeutics, The Macmillan Co., New York, 1941. 3. Osol, A. and Farrar, G. E.: Dispensatory of U.S.A., J. B. Lippincott Co., Philadelphia, 24th ed., 1947. 4. Sollmann, T.: A Manual of Pharmacology, W. B. Saunders Co., Philadelphia, 7th ed., 1948. 5. Loc. cit., p. 750.

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A. M. A. WARNS OF HEALTH HAZARDS IN USE OF PESTICIDES

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"Studies indicate that already many constituents of the American diet may be contaminated with materials of unknown toxicity used to destroy insect pests or weeds," says an editorial in a recent issue of *The Journal of the American Medical Association.*

"The insecticides," the editorial states, "include those materials which have been long in use such as lead arsenate, nicotine and fluorine compounds, and new materials, about which little is known, such as the organic phosphates, chlordan and many others, and DDT."

The Council on Foods and Nutrition of the American Medical Association states that the chemical contamination of foods with residues of these substances is but a part of the broader problem created by their wide use, for in addition to the danger from ingestion, the effects of inhalation and skin absorption must be determined.

The council in a separate article in *The Journal* says it recognizes the potential usefulness of newly-developed pesticides and herbicides, but at the same time it recognizes also the potential hazards to individual and public health of the unrestricted use of these products which are placed on the open market

(Continued on Page 60)



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Loryngoscope, Feb. 1935, Vol. XLV, No. 2, 149-154; Laryngoscope, Jon. 1937, Vol. XLVII, No. 1, 58-60; Proc. Soc. Exp. Biol. and Med., 1934, 32,241; N. Y. State Journ. Med., Vol. 35, 6-1-25, No. 11, 590-592.

A. M. A. WARNS OF HEALTH HAZARDS IN USE OF PESTICIDES

(Continued from Page 58)

before they have been adequately studied and their toxicologic properties determined.

"It is obvious," the council says, "that controls must be placed on the sales and distribution of products of unknown or incompletely known toxicity. The time to establish controls, voluntarily or otherwise, is now, before possible tragic consequences occur."

The Council on Foods and Nutrition, in conjunction with the A.M.A. Council on Pharmacy and Chemistry, is planning a meeting some time this fall with officials of the U. S. Department of Agriculture, the U. S. Food and Drug Administration, the U. S. Public Health Service, other governmental agencies and other organizations and agencies to consider the problem of food contamination with pesticides.

"The brands of new insecticides, fungicides, and herbicides—weed killers—now on the market or contemplated, number several thousand," *The Journal* editorial says, adding:

"Little is known about either the acute or chronic pathologic effects on man of these new pesticides. When pesticides are poisonous to insects they are usually poisonous to man. Their true value depends on a significant difference between the toxic effect on man and insects.

(Continued on Page 64)

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A. M. A. WARNS OF HEALTH HAZARDS IN USE OF PESTICIDES

(Continued from Page 60)

"Voluntary control by producers and distributors of these substances should be instituted immediately. If voluntary control proves to be inadequate for the protection of the public, suitable legislation must be considered and effective means of control promptly established. Prompt voluntary action by the industry is imperative.

"Even though added controls may impede the development of pesticides, there are essential precautions which must be taken in order to avoid the danger of mass poisoning, which might well offset the potential benefits of the new agents."

Dr. James R. Wilson, Chicago, secretary of the A.M.A. Council on Foods and Nutrition, said in commenting on *The Journal* editorial that some companies which manufacture these products have taken no responsibility, but have passed responsibility on to the buyer.

In studying the problem, the council found, for example, that one company promoted its insecticide with this note of caution: "Avoid inhalation of dust. Avoid contamination of foodstuffs. Seller makes no warranty of any kind, express or implied, concerning the use of this product. Buyer assumes all risk of use or handling, whether in accordance with directions or not."

Dr. Wilson urged housewives to wash all fruits and vegetables thoroughly before eating, suggesting also that home gardeners should carefully observe all available instructions.

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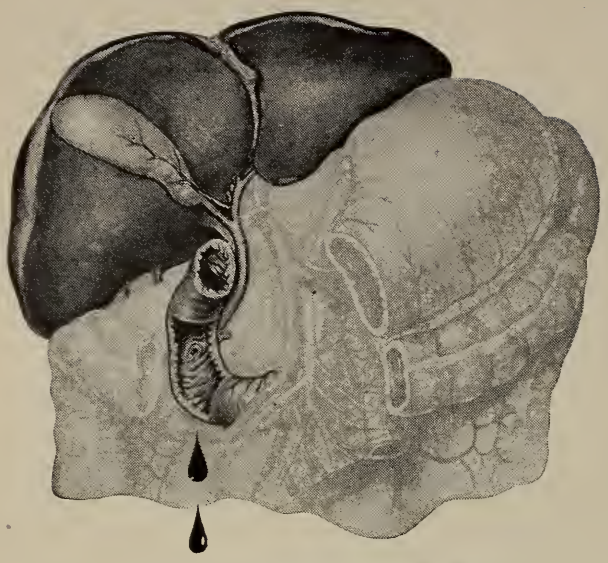
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*Albrecht, F. K.: Modern Management in Clinical Medicine, Baltimore, The Williams and Wilkins Co., 1946, p. 170.

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CITES IMPORTANCE OF EARLY DIAGNOSIS IN STOMACH CANCER

The time has come to abandon the old attitude of hopelessness toward cancer of the stomach and esophagus, declares Richard H. Sweet, M.D., visiting surgeon at the Massachusetts General Hospital, Boston, Mass.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Sweet says that "cancer of the stomach can be cured in an appreciable number of cases," provided that an early diagnosis is made and that the growth is of a reasonably favorable type.

Attitudes toward cancer of the esophagus are also changing, he indicated. Pointing out that until recently this type of cancer was considered quickly fatal in all cases, Dr. Sweet reports that "an appreciable number" of patients with cancer of the esophagus now survive three years or more because of advances in surgery.

Earlier diagnosis, lower operative mortality, and a widening of the scope of the operation for cancer of the stomach have presumably cured a larger number of patients with stomach cancer in recent years, he says.

Cancer of the stomach has long been regarded as a common disease. Cancer of the esophagus is also a common disease from which about 27,000 persons die annually in the United States, according to Dr. Sweet. As an estimated 40,000 persons die each year in this country from cancer of the stomach, the two types cause nearly 21 per cent of the total deaths from cancer in the nation.

Statistics have shown a one-sided picture which is unduly discouraging to patients with cancer of the stomach, Dr. Sweet emphasizes. Latest reports from various clinics show that 20 to 30 per cent of patients operated on for the disease are living five years after the operation, he says, explaining:

"Statistical studies from various sources show that of all patients with proved cancer of the stomach, not over 5 per cent survive five years or more, and then only as a result of the application of surgery.

"To be influenced by this apparently discouraging result, however, is to place emphasis on the wrong aspect of the problem. The fact that, of all cases of cancer of the stomach in which a diagnosis has been made, in only 5 per cent a cure is effected, indicates that a large percentage of the cases are unsuitable for surgery when the patient is first seen or too far advanced for cure even though surgical excision is attempted. There are innumerable statistics to prove this contention."

Massachusetts General Hospital statistics show six types of stomach cancer. More than 90 per cent of patients operated on for the most favorable type were living five years or more after the operation.

Of the second most favorable type, 75 per cent were living five years after operation, and of the third and fourth most favorable types, 40 per cent were living five years after operation.

The most frequent type of stomach cancer, advises Dr. Sweet, is the adenocarcinoma, the third most favorable.

The outcome of both cancer of the stomach and

(Continued on Page 12)



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CITES IMPORTANCE OF EARLY DIAGNOSIS IN STOMACH CANCER

(Continued from Page 12)

Onset of cancer of the stomach is often insidious and the early symptoms are often vague, he points out. Only sometimes is pain felt; more obscure symptoms are discomfort, indigestion, or a bloated or full feeling after eating.

Since the accuracy of x-ray films in diagnosing cancer of the stomach is not more than 90 per cent with even the most expert technicians, according to Dr. Sweet, he recommends inspection of the interior of the stomach with a gastroscope or esophagoscope.

Cancer should be suspected in every case of gastric ulcer which does not heal completely under treatment within a short time—one month at the most—Dr. Sweet cautions.

FORRESTAL APPROVES INTEGRATION OF PANAMA CANAL ZONE HOSPITALS

Secretary of Defense James Forrestal has approved integration of National Military Establishment hospital and medical services in the Panama Canal Zone area, according to a news item which appears in a current issue of *The Journal of the American Medical Association.*

Approval was given on recommendation of the committee on medical and hospital services of the armed forces.

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DOCTORS REPORT SPEEDY TEST FOR SICKLE-CELL ANEMIA

A rapid test to demonstrate the sickling process in blood, whereby the red corpuscles acquire a sickled, or crescent-like shape, is reported by Karl Singer, M.D., and Sidney Robin, M.D., in a recent issue of *The Journal of the American Medical Association.*

The two doctors are from the Department of Hematologic Research and the Kunstadter Laboratory for Pediatric Research, Michael Reese Hospital, Chicago.

Sickle cell anemia, which results from the sickling phenomenon, is, in the words of the authors, "a great masquerader," manifesting itself in several different ways. Often, according to the article, sickle cell anemia may be confused with perforated ulcers, rheumatic fever, tuberculosis, or skin and nerve diseases. The disease is confined principally to Negroes and the tendency to it is hereditary.

Because of these diagnostic pitfalls, the authors state that "the need for routine examinations for the sickling phenomenon has been emphasized repeatedly," adding that "particularly in the dramatic surgical conditions a rapid test is urgently needed."

(Continued on Page 22)



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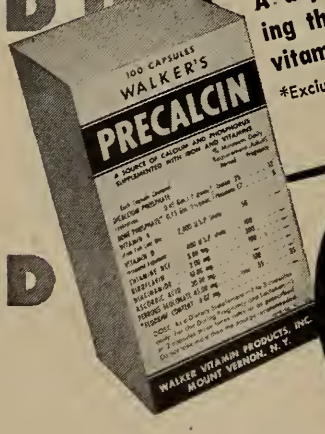
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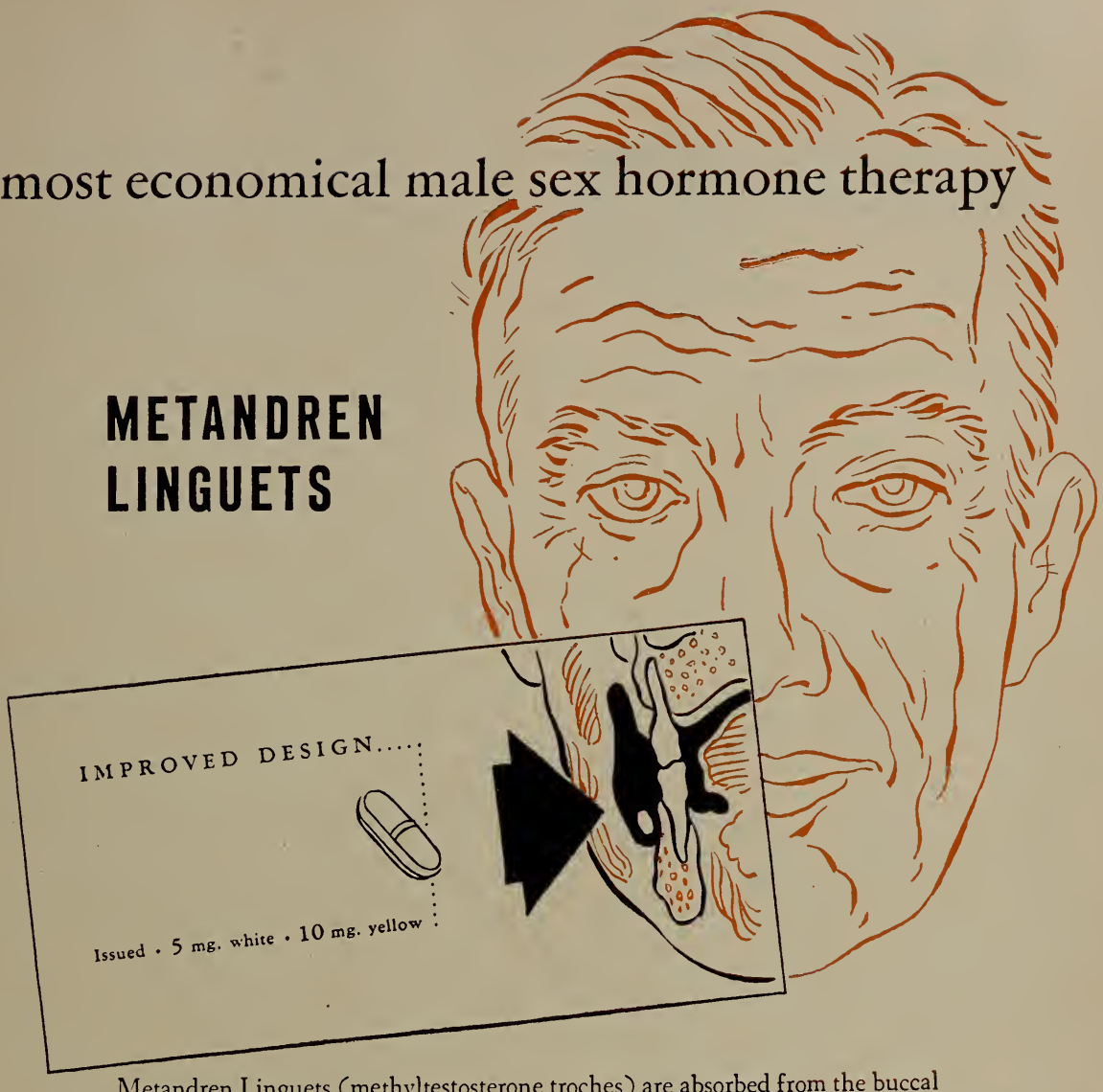
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But here's the punch line! While we were sharing a pot of hospital coffee, that same doctor did ME a favor—by talking about the difficulties of administering multiple 10 cc. doses of unconcentrated serum to infants.

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Lapin (writing in the Journal of Pediatrics) puts the comparison in clinical terms ". . . administration of a 10 cc. volume (lyophilized residue of 20 cc. of human serum resuspended in 10 cc. of diluent) is painful. Repetition of this 10 cc. dose at frequent intervals becomes a struggle . . . With a ten fold concentration, the immune bodies of 25 cc. hyperimmune pertussis serum can be delivered in 2.5 cc. of the globulin fraction, in an ordinary hypodermic injection."

→With 10-fold concentration in a 2.5 cc. dose Hypertussis* offers ". . . by far the most rational therapeutic agent yet used in the treatment of whooping cough." (Silverthorne's statement at the A.M.A. Section on Pediatrics, last year)

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TYPHOID DEATH RATE DECLINING STEADILY IN LARGE U. S. CITIES

Typhoid fever deaths in 93 large U. S. cities have shown a steady decline from 85 in 1943 to 57 in 1947, according to the 34th annual report appearing in a recent issue of *The Journal of the American Medical Association.*

In the 78 cities for which data have been available since 1910, the report says, there occurred 53 deaths from typhoid in 1947, 54 in 1946, 80 in 1945, and 66 in 1944. This provides a rate of 0.15 per hundred thousand of population for 1947, the same as last year's figure for 1946, which was a new low.

Figures for the report were obtained from local health officers, who were asked to record an estimate of population.

The number of cities with no death from typhoid during the past two or more years has increased from 25 in 1941 and 41 in 1945 to 49 in 1946 and 1947. Fort Wayne continues to head the list with no death in 13 years. Duluth, Springfield, and Yonkers have clear records for nine years, and Canton, Erie, Grand Rapids, and Tulsa report no death from typhoid in eight years. South Bend, Fall River, and Hartford have had no deaths from typhoid among residents for 12, 11, and nine years, respectively.

The number of cities with no deaths from typhoid has increased from 60 in 1946 to 65 in 1947. Charlotte, Gary, and Sacramento, not included in the group of 93 cities, also report no death. Detroit, Baltimore, San Antonio, San Diego, Fort Worth, Hartford, Memphis, Salt Lake City, and Fall River report no deaths among residents. The number of cities with rates of less than 1.0 has increased by three (91 in 1947), and there remain only two cities with a rate of 1.0 or more. While in 1946 there was no city with a death rate in excess of 2.0, in 1947 there was one such city, Miami (2.3 per hundred thousand). Forty-seven cities (49 with Charlotte and Gary) record no typhoid death in 1946 and 1947.

The New England cities with a population of 2,579,152 which set an all-time record with no deaths from typhoid in 1946, did not even maintain first place in 1947 and were outranked by the Middle Atlantic and East North Central cities. The rates in the latter two groups were 0.05 each, and the New England groups report a rate of 0.08.

The East South Central cities climbed from last place in 1946 and 1945 to fourth place in 1947 with a new low rate of 0.23. The West North Central cities follow close behind with 0.26, a large increase over the 1946 rate (0.07). The Mountain and Pacific cities record a slight rise (0.31 to 0.33), and the South Atlantic cities came up from last place in 1946 (0.44) to next to last (0.37) in 1947. The West South Central cities are last with the same rate as in 1946 (0.39).

Sixteen of the large Middle Atlantic cities (there were 13 in 1945, 12 in 1946) with a population of 13,129,185 report no death from typhoid in 1947. These cities report the lowest group rate (0.05) for 1947, followed by a fraction when computed to the third decimal by the East North Central cities. It is considerably lower than the rate for 1946 (0.11) and lower than that for 1943 (0.08).

(Continued on Page 22)

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DOCTORS REPORT SPEEDY TEST FOR SICKLE-CELL ANEMIA

(Continued from Page 17)

The present methods of examining the sickling process are inadequate, according to the authors, because "they do not provide the required information with sufficient rapidity and reliability."

In the rapid test devised by Drs. Robin and Singer, a drop of the suspected blood is mixed with a drop of cloudy broth culture of non-disease-breeding bacteria and then sealed. Thus, according to the article, "the living organisms consume oxygen rapidly and also give off carbon dioxide, . . . creating the most favorable conditions for the detection of sickling tendencies." . . .

TYPHOID DEATH RATE DECLINING STEADILY IN LARGE U. S. CITIES

(Continued from Page 20)

New York records a new low mark, with only 2 deaths. The previous low was in 1943, with 4 deaths. In 1946 there were 8 deaths.

The rate for the South Atlantic cities (population 2,727,985) is higher than the low rate for 1944 (0.22), but is lower than the rate for 1946 (0.44) and that for 1945 (0.62). In these cities there occurred 10 deaths in 1947 (six among residents) and 12 in 1946 (nine among residents).

The East North Central cities (population 9,386,378) are in virtual tie with the Middle Atlantic cities

(Continued on Page 26)

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TYPHOID DEATH RATE DECLINING STEADILY IN LARGE U. S. CITIES

(Continued from Page 22)

for first place. The number of deaths from typhoid decreased from six in 1946 (33 in 1940) to five in 1947, a new low, and the rate from 0.35 in 1940 and 0.06 in 1946 to 0.05 in 1947.

The six cities in the East South Central group (population 1,286,747) show a decrease (0.23 in 1947, 0.54 in 1946, and 0.70 in 1945) in the death rate that marks a new low record, the previous one being 0.31 in 1944.

The West North Central cities (population 2,716,484) show an increase in the number of deaths from two in 1946 to seven in 1947. Five of the seven were among residents. The death rate increased from 0.07 in 1946 (it was 0.11 in 1943, 1944, and 1945) to 0.26 in 1947.

The eight West South Central cities (population 2,048,692), report the same number of deaths (eight) as for 1946. The rate of 0.39 in 1947 is in contrast to the rate of 2.00 in 1940. Notwithstanding this continued reduction, the rate for this group of cities is the highest for all groups.

The 11 cities (excluding Sacramento) in the Mountain and Pacific states (population 4,186,039) report an increase of one death (13 in 1946 and 14 in 1947). The rate has increased from 0.17 in 1945 to 0.31 in 1946 and to 0.33 in 1947.



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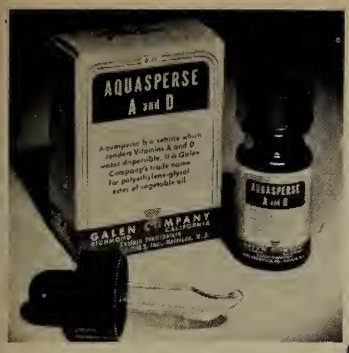
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A new technique of treating club foot with a cohesive bandage gives most babies born with the deformity a normal foot, says Emil D. W. Hauser, M.D., of Chicago.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Hauser points out that treatment with the bandage, which will not adhere to or irritate the skin, can be begun immediately after birth.

"A summary of results in 70 patients treated during a period of six years clearly established the advantages of this type of treatment," he comments.

The earlier treatment of clubfoot is begun, the better the correction that will be obtained, he emphasizes, as the younger the child the more rapid is growth and the softer and more easily changed are structures of the foot. With former methods, such as the use of plaster casts and splints, treatment could not be begun until a baby was from one to three months of age, he says.

The entire foot and leg are covered with the cohesive bandage and a reinforcement of adhesive tape to hold the foot in as nearly a normal position as is possible.

"The interval between changes of bandage is variable, depending on the age at which the correction is started and the severity of the deformity," says Dr. Hauser.

(Continued in Back Advertising Section, Page 38)

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What's New in Communicable Diseases

EDWARD B. SHAW, M.D., *San Francisco*

THE essential concept of the control of communicable diseases is fast changing with advances in knowledge of their transmission. Quarantine, previously emphasized, has become less important. Quarantine has been shown to be of little real value in the control of diseases of high contact communicability (measles, chicken pox, smallpox). It is of little significance in those diseases in which the spread of infection is less direct (meningococcus disease, streptococcosis, poliomyelitis, typhoid, diphtheria) where the agency of transmission involves subclinical infection and the carrier state and when isolation is imposed only upon the obviously ill. Isolation of the patient is even less of value in the control of insect-borne viruses and rickettsiae (encephalitis, typhus, Q fever).

The origin of communicable disease hospitals was the pest house, which was for the segregation of the ill from the well and not for the protection of patients from one another. The newly developed concept is for individual isolation consistent with the methods of transmission and the development of aseptic nursing by which the patient may be appropriately isolated almost anywhere, except that those diseases of extremely high contact communicability (measles, etc.) can scarcely be controlled by any manner of precaution.

The communicable disease hospital has developed away from the pest house and now exists best as a fever hospital where transmission is controlled by precautions on the part of the personnel and where the emphasis is upon superior facilities for therapy rather than enforcement of absolute quarantine. The problem of communicable disease has become identified with the general problem of infectious disease.

Read as part of Panel Discussion on What's New In Pediatrics at the 77th Annual Session of the California Medical Association in San Francisco, April 11-14, 1948.

The public has been indoctrinated in the employment of precautionary measures with resultant avoidance of many common infections during childhood. This has resulted in spreading childhood infections over a larger period of the life span and has led to some curious effects from the occurrence of these diseases in adult years. It has been seriously proposed that under primitive conditions exposure to the virus of poliomyelitis occurred commonly in infancy at a time when resultant disease was silent or non-paralytic and that better protection has caused this disease to assume epidemic proportions in older age groups with paralytic sequellae.

German measles is traditionally a childhood disease of no great significance. Its increased occurrence in older age groups has provided the evidence of its dismal effects on the fetus when it occurs early in pregnancy. This disease is more benign at an early age.

Newer methods of therapy have greatly modified the course of many infections. Antibiotic therapy and chemotherapy have caused the treatment of infections due to the streptococcus, meningococcus, pneumococcus, and other organisms to be greatly improved and simplified. Meanwhile latent effects of antigen stimulation have become recognized as important in the production of late sequellae. This applies strongly to streptococcal diseases in which rheumatic sequellae are seen long after the stage of acute pyogenic infection and is doubtless significant in many other infections, possibly serving to explain some of the late complications of virus infections such as the encephalitides which complicate the exanthemata.

Certain infections have been little influenced by new methods of therapy. Diphtheria is demonstrably best controlled by immunization and best treated by antitoxin. Warnings of increased incidence point mostly to greater morbidity and mortality in older

age groups past the effect of immunization. The actual value of sulfonamides and antibiotics has not been acceptably proved even in the carrier state.

Scarlet fever is rapidly coming to be regarded as only a part of the general problem of streptoccal disease in which the eruption does not notably indicate increased communicability. Immunization has not encouraged general acceptance; serums which are potent against the erythrogenic toxin are little used and treatment seems best served by penicillin and sulfonamides.

In measles unmodified human serum for prophylaxis has encountered the newly recognized risk of homologous serum hepatitis which is inherent in all such preparations. Gamma globulin affords better protection without this danger. It has become apparent that modified measles does not unfailingly protect against future exposure and I believe that it is not certain that modified measles is exempt from post-measles encephalopathy. The prophylactic value of penicillin and sulfonamides against secondary invaders in measles is uncertain and probably unjustified.

Meningococcus disease is amenable to therapy with sulfonamides, which is the agent of choice far above former therapeutic measures.

Whooping cough has shown an overall increased incidence although most of us can point to diminution to the vanishing point in practices in which patients are 100 per cent immunized. Statistical evidence of the value of immunization will be affected only by early universal vaccination in which lowered exposure rates will augment the effect of varying degrees of immunity.

Poliomyelitis is not susceptible to any of the new antibacterial agents for prophylaxis or treatment, perhaps because this minute virus has little in common with the life processes of larger viruses and bacteria. This problem demands a new and imaginative approach not comprehended in our philosophy. The epidemiology of poliomyelitis indicates the absence of a sequence of exposure, incubation period, disease and immunity comparable to better understood infections. Host susceptibility is quite as important a factor as the study of the virus itself.

The arthropod-borne viruses of the encephalitides have assumed increasing importance and, although knowledge of the vectors and their control has increased, little has been added to specific therapy.

To the problem of influenza has been applied the mass administration of virus vaccines. Failures of protection have been encountered with respect to certain strains. This poses a neat problem in the selection of strains for future vaccination, especially against such a pandemic as occurred 30 years ago. The propriety of the use of influenza vaccines in the private practice of pediatrics seems dubious to me in view of their uncertain action, the short period of potential protection and the possibility of egg protein sensitization.

Rickettsial infections have assumed increasing importance. Typhus and kindred infections have been encountered throughout the United States. Rickettsial pox was identified in apartment houses in New York City—of all places! The year's prize for interesting medical writing would be awarded by me to *The New Yorker* for its account of this disease. Q fever, which couldn't happen here, did—in Texas and in California. The study of the vector problem in these diseases is of great magnitude. It may certainly be suspected that many disease problems of this nature await only a deft and inquisitive approach.

The use of paraminobenzoic acid in the therapy of certain rickettsial diseases has provided us with an entirely new therapeutic approach in which interference with the enzyme systems upon which the life processes of these organisms depend is a principle which may be susceptible to much further extension.

The recent studies on histoplasmosis indicate that a widespread form of infection simply awaited study and recognition; and the increasing frequency with which toxoplasmosis has been recognized, often in early infancy, indicates the probability that latent infection of this nature may be far more common than we suspect.

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QUESTIONS AND ANSWERS

Question: When do you advise the use of immune globulin in measles prevention? (Prevention referring both to complete protection and modification with a comment on dosage.)

DR. SHAW: This question might provoke a general discussion with some differences of opinion. My own practice is not to use globulin at all under six months of age and to use it sparingly between six months and one year. Usually until the age of six months the infant has a certain amount of residual immunity which is either transplacental specific immunity or consists of a relative insusceptibility to this infection at this age and this factor suffices to protect to a variable degree during the second six months. From one to three years of age I usually employ gamma globulin in an effort to produce modification in a child who is otherwise healthy. 0.025 to 0.02 cc. of gamma globulin per pound of body weight given on the day of appearance of the rash in the child to which the patient has been exposed will pretty reliably result in mild modified measles. There are some individual differences in susceptibility, and the intensity of exposure is another factor which affects the success of the procedure. It is impossible to predict the exact results and sometimes this dosage fails to protect and occasionally results in complete protection rather than modification. The exact degree of permanent protection which is conferred by a modified attack of measles is also variable and is somewhat dependent upon the degree of symptoms—the more evidence of disease which is present, the more likelihood there is of enduring immunity.

In the age period of over three to perhaps four years of age I am sufficiently old-fashioned simply to permit the child to go ahead and have measles and thus develop permanent protection. In the presence of other infections and in the convalescent stage of other respiratory infections, doses somewhat in excess of the above should routinely be employed for complete protection against the present exposure.

Question: Is immune globulin of definite value in the treatment of measles after the rash erupts, particularly in children under the age of two years, and if so, what dose do you use?

Dr. Shaw: I think this is a most important question. We have just had a patient who was admitted to the hospital with rather severe scarlet fever, and on the eighth day after admission he developed measles—we at least had the assurance that he was not exposed in the hospital. This child was given 10 cc. of gamma globulin, which corresponds to about 250 cc. of immune serum, and he proceeded to have a very mild attack of measles which I think was definitely the result of the gamma globulin administration. I believe there are many times when this principle of treatment should be employed. Toomey has shown that if sufficiently large amounts of convalescent serum (or globulin) are given during the early stage of measles, considerable modification can be effected even if this is done only a short time before the rash appears. This procedure is most useful when symptoms of measles appear during the course of another infection or in the surgical patient or at any time in which full-blown measles is most disadvantageous. I think this is an interesting contradiction of the statement by Rivers that in virus diseases nothing can be accomplished, once symptoms are evident (Rivers happened to be talking about the serum therapy of poliomyelitis), to modify the course of such a disease because of the intracellular habitat of the virus. Under these circumstances, measles can be modified if sufficient amounts of an immune serum principle are employed and I have seen the same thing happen more or less inadvertently in the course of chicken-pox in which transfusions were administered just as the very first eruption appeared. In these cases the first few vesicles appeared and following the transfusion these vesicles rapidly regressed and practically no other eruption was evident.

Question: Why has the use of immune globulin eliminated the danger of serum hepatitis?

Dr. Shaw: I don't know—except that while the virus is potentially present in the whole serum it may be eliminated by the processing which results in purified gamma globulin. Furthermore there is some concentration of antibodies against the hepatitis virus in pooled gamma globulin preparations. Even in pooled serum preparations in which processing has not eliminated the virus of hepatitis the coincident presence of antibodies against the hepatitis virus may be the factor which results in inhibiting the appearance of symptoms for such a long time after the whole serum is administered. There was a publication during the past week which you have doubtless all seen, pointing to the fact that the presence of virus and immune substance in the same preparation was sometimes responsible for a long incubation period. This same phenomenon is sometimes seen in measles prophylaxis in which very small doses of immune serum or globulin are given, under which circumstances measles may appear after a prolonged incubation period instead of complete protection. Conceivably if a pooled specimen of serum or plasma contains small amounts of the virus of hepatitis as well as small amounts of antibody, homologous serum hepatitis may follow after an incubation period of 90 to 120 days.

Question: Inasmuch as it is difficult to tell when a child will be exposed to measles, how about exposing him deliberately and then giving immune serum globulin to modify the attack?

Dr. Shaw: I would not do this. I am not sufficiently hardy to expose a child definitely to measles and thus take the responsibility for whatever might occur and I am not confident that the dosage of gamma globulin could unfailingly be selected so as to provide the child on the one hand with minimal measles and on the other hand with permanent immunity. Many of the patients who have had modified measles in childhood secured through the use of gamma globulin after exposure have only a transient succeeding immunity and later on may be completely susceptible to the disease. I am afraid that many of those whom we have thus protected in childhood will be fully susceptible in adult years. We may see many curious things with a lot of pediatrics relegated to adult medicine in later years.

What's New in the Field of Immunization

JOHN J. MILLER, JR., M.D., *San Francisco*

IN the field of immunization there have been a number of recent developments which are worthy of discussion. Mumps can be added to the list of diseases which in the future may be prevented. The studies of Stokes, Enders, and their associates[27,5] are encouraging. In experiments, formolized mumps virus from monkey parotid glands protected about 50 per cent of children against infection. Attenuated virus from egg passage may eventually prove to be the answer.

The somewhat precarious status of two older immunization procedures has been altered in the past year. The outlook for successful immunization against influenza has become less promising. Contrary to earlier studies made in United States Army camps, three field trials reported during the past year yielded no evidence of protection.[6,30,26] These failures are in the main accounted for by the appearance of new strains of virus antigenically distinct from those incorporated in commercial vaccines. Unfortunately, there is also reason to believe that new strains will continue to appear. As the immunity conferred is apparently almost strain-specific, vaccines in the future either must be highly polyvalent or broadly antigenic, or may even have to be produced rapidly in the face of a spreading epidemic after the infecting strain has been isolated. The one cheerful aspect of the present status of vaccination against influenza is the likelihood that calcium phosphate adsorbed vaccine[25] will produce a firmer and more lasting immunity than do the currently available unadsorbed products.

The controversial status of BCG vaccination against tuberculosis, on the other hand, seems to be resolving. Recent reports from the Indian reservation,[1] from Denmark,[12] and from Chicago,[22] have demonstrated that decreased morbidity and mortality rates can be obtained with some preparations of vaccine. The evidence has been considered sufficiently valid by the United States Public Health authorities to lead them to commence further field studies and to attempt laboratory standardization of the vaccine.[29] The Surgeon General's office, however, does not feel that BCG vaccine should be made commercially available at present. Public health officials desiring to set up controlled studies should contact the office of the Tuberculosis Control Division of the U. S. Public Health Service and obtain vaccine through this channel.

Now, a word about the oldest immunization procedure. There is widespread and misplaced confidence in the validity of the "immune reaction" to cowpox vaccine. It has long been known[4] that local erythema and induration appearing in 24 hours may result from inoculation with dead virus in an individual allergic to calf lymph. Nevertheless, the occurrence of smallpox in American and British soldiers with records of recent "immune reactions" has jolted our complacency.[4] Leake in the U. S. Public Health Service handbook on vaccination[16] describes the "early reaction" as one in which "the broadest redness is reached in 8 to 72 hours after vaccination." There is "a slight elevation of the skin . . . and usually no vesicle." He then goes on to state that "such a reaction should not be called a reaction of immunity unless fully potent vaccine has been used." But how are we to know our vaccine is fully potent? The only answer is: By observing instances of primary local vaccinia following inoculation with the same lot of vaccine at about the same time. The best that we can do, then, is to obtain new lots of vaccine frequently and always keep them in the freezing chamber of a refrigerator.

In diphtheria immunization there are still problems—that of the susceptible adult and that of the individual who is sensitive to the toxoid. Commonly these two problems coexist. Toxoid sensitivity tests are essential before toxoid is given to adolescents and to adults. It is possible that the sublingual application of toxoid tablets[2,20] will in the future prove of value in reimmunizing the toxoid-sensitive adult.

In the field of pertussis immunization there has been no substantial contribution since Sako and his coworkers[24,23] showed that infants under three months of age could be actively immunized. The question of whether precipitated vaccine is necessary for immunization at this age has not been settled.

Active immunization against tetanus has such a splendid war record that unwarranted statements have appeared in the literature. It has been said that when a previously actively immunized individual is wounded, all one need do is to give him a "booster" of tetanus toxoid. This complete confidence in primary immunization and in the secondary anamestic response requires a dash of cold water, in my opinion. The very great protection against tetanus obtained by the armed forces was in men very recently immunized. The majority of troops also had had routine annual "booster" reinjections.

The effect of the lapse of time on the speed of the response to reinjection of toxoid is not well known. Contrary to the reports of others,[21,19] we have observed that with the passage of time the speed of response is decreased. In some individuals, after an interval of five years or more since the last previous injection there may be no detectable antitoxin seven days after the reinjection. Furthermore we have observed that children basically immunized with pre-

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From the Department of Pediatrics, Stanford University School of Medicine, San Francisco, California.

cipitated or adsorbed toxoid respond to a "booster" faster than do those basically immunized with fluid toxoid. Thirdly, and on the other hand, fluid toxoid produces a more rapid increase in antitoxin than does precipitated toxoid in children basically immunized with the latter. In other words the immunization mechanism is sensitized better by a slowly absorbed antigen but is stimulated faster by a rapidly absorbed antigen.

One may ask, "Are these measurements of antitoxin significant?" I believe so, for the following reasons. Let us examine the few cases of tetanus that did occur in immunized soldiers during the recent war. A total of 28 cases have been reported from the British and American armies.[3,17] All cases occurred after severe wounding, and almost all occurred after unusually short incubation periods—the shortest was two days. The fatality rate in these few cases was surprisingly high, 50 per cent. Apparently what occurred was that active immunization prevented tetanus in everyone except those suffering from massive intoxication following severe wounding. Here the incubation period was too short for a booster to stimulate antitoxin production. When the British gave prophylactic antitoxin in such cases, they obtained a lower fatality rate than we did with toxoid "boosters."

If both antitoxin and toxoid could be administered in such severe cases, would both immediate and delayed protection result? From evidence obtained in our laboratory, I believe so. Studies following the simultaneous administration of antitoxin and toxoid in different extremities of previously immunized animals indicate that the secondary immune response, unlike the primary immune response, is not prevented by circulating heterologous antitoxin. In summary, then, it would appear that maximal protection against tetanus can best be obtained by (a) inducing basic immunity with precipitated toxoids, (b) maintaining high levels of antitoxin with routine biennial reinjections of precipitated toxoids, and (c) employing rapidly absorbed fluid toxoid when wounding occurs. In cases of compound fractures or other wounds likely to be massively contaminated, or in cases in which the interval since the last toxoid injection is five years or more, prophylactic antitoxin should probably be administered in addition to the booster at the time of wounding.

In regard to passive immunization procedures, what's new, of course, is gamma globulin. In addition to being highly effective, and the agent of choice, in the prevention of measles, it has been employed in three other virus diseases. In mumps it is apparently not effective unless prepared from mumps convalescent serum,[8] which is not commercially available. On the other hand, ordinary gamma globulin from normal adult serum has been reported to confer protection against chickenpox.[7] Should this be confirmed, we will have a very useful agent in protecting sick infants and children exposed in hospitals.

In epidemic and endemic viral hepatitis ordinary gamma globulin is effective if administered during the first two weeks after exposure. Its great value was clearly demonstrated in two institutional epidemics[28,11] and in a large epidemic among our troops in Italy.[9] The dose for children is 0.22 cc. per kg. of body weight.

The importance of preventing the spread of epidemic hepatitis in troops at war or in children in an institution is obvious. But should we attempt to protect the child who has been exposed at home or in school? An attack of viral hepatitis produces immunity which is not strain-specific.[10] On the other hand, there is now ample evidence[15] that this disease is not always benign. Fatal cases are extremely rare but permanent liver damage may result.[18] Repeated needling of the liver for biopsy specimens is reported to have shown transition from acute hepatitis to cirrhosis in a few instances.[14] Fortunately for pediatricians, chronic liver disease following hepatitis is far more common in adults than in children.[13] Nevertheless we have recently observed a case of portal cirrhosis in a 12-year-old boy who had had an attack of typical catarrhal jaundice nine months previously. No other possible contributory factor was found. It is my opinion that although the dangers of infectious hepatitis are remote in childhood, this preventable disease should be prevented by passive immunization whenever possible.

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QUESTIONS AND ANSWERS

Question: Why not three doses of toxoid for basic immunity?

DR. MILLER: There is evidence that basic courses of three injections of precipitated tetanus toxoid induce higher and more enduring titers of antitoxin than do courses of two injections.

Question: Is not a recall injection of toxoid preferable to antitoxin?

DR. MILLER: Yes, indeed, for thereby sensitization to horse serum is avoided. A recall injection of toxoid can be relied upon and should be employed in previously immunized individuals for all puncture wounds and common lacerations. As I have already stated, antitoxin need be considered only in cases of compound fractures, massively contaminated wounds, shock (in which the immune response may be impaired), and when the interval since the last injection of toxoid is five years or more. Under these conditions I believe antitoxin should be administered in addition to toxoid. The antitoxin will afford immediate passive protection against short incubation period tetanus while the patient's immune mechanism is mobilizing his own antitoxin.

Question (Moderator): How much antitoxin, Dr. Miller?

DR. MILLER: Five thousand units if the patient is in shock, or severely wounded. Fifteen hundred units if the time interval since the last injection of toxoid is five years or more and the wound is not severe.

Experimental Use of Testosterone Compounds in Premature Infants

E. Kost Shelton, M.D., and Jerome S. Mark, M.D., *Los Angeles*

PREVIOUS laboratory investigations have indicated that the premature infant has many metabolic defects. In particular there are inadequacies in nitrogen, calcium, and phosphorus storage; faulty ability to absorb fat; and multiple requisites conditioned by the rapid rate of growth. Since nitrogen storage and utilization are in part the physiological effects desired, it occurred to us that testosterone, one of the most important metabolizers of nitrogen, might be a rational drug to employ as an adjunct in the care of certain premature infants.[3]

During the past year infants of both sexes on the premature wards of the Los Angeles County General Hospital received various testosterone compounds and the effects were observed. The materials considered suitable for such a study were the methyl derivatives for oral use, and the propionate derivatives for intramuscular administration. Methyl testosterone is obtainable in tablet form which can be crushed and introduced directly into the formula, or as a propylene glycol solution which may be dropped directly under the tongue. Without precedent the dose of methyl testosterone was arbitrarily set at 5 mg. daily. It was found that the propylene glycol solution lent itself more readily to administration. Testosterone propionate was given intramuscularly in 4 mg. doses daily. Treatment in both series was begun at 12 hours after birth and continued for three weeks.

The infants observed weighed under 2000 grams and for each group there was a similar group of the same age and weight, under the same general care, as control. Daily observations were made of the weight, alertness, type of stool, amount of lanugo, size of clitoris and penis, and the number of erections. These, in addition to the length of time required to regain the birth weight, and that required to gain to 2500 grams in body weight were used as the ultimate basis for evaluation.

To date there has been a total of 74 patients which have been under observation for a year. These infants, of both sexes, to which both types of testosterone compounds were given, have been divided into two groups, those weighing between 1000 and 1500 grams and those between 1500 and 2000 grams at birth. A significant indication of the benefits obtained by the use of both testosterone compounds was evident by the enhanced welfare of the treated prematures in both weight classifications. In the 1000 to 1500 gram weight groups an average of 14.7 days was required by the untreated controls to regain their birth weight. Those on methyl testosterone in the same weight group required an average of 9.0 days; and those on testosterone propionate only 7.5 days. Thus comparison between the treated and the control group reveals a 50 per cent reduction in the time required to regain birth weight. Similar results were obtained in the 1500 to 2000 gram group. It was also found that whereas the controls required 42 days to gain to 2500 grams, those to whom the propionate was administered required only 35 days and those receiving the methyl compound only 32 days to reach this same level. Again these treated prematures revealed a significantly earlier attainment of maturity when compared with their untreated controls.

An even better indication of the benefits derived from the use of testosterone compounds was obtained from the study of four sets of twins. Here the larger of the two, the one with the greater chance for survival, was used as the control while the smaller was given testosterone. All of the twins on the testosterone compounds, who theoretically should have taken longer to regain their birth weight, did so in a much shorter period than their larger more mature control siblings. In fact, in three of the four sets, the birth weight was maintained from the onset of treatment while in the fourth there was an approximate 50 per cent reduction in the anticipated number of days required to regain the birth weight. Here again the days required to gain to 2500 grams showed a reduction in the twin treated with testosterone in three out of the four, while in the fourth set only two days longer was required to bring the smaller infant to maturity.

It is now generally accepted that testosterone compounds cause a decline in urinary nitrogen reflected in the urea fraction, unaccompanied by an increase in the plasma protein, non-protein nitrogen, or hemoglobin concentrations.[1] As there is no change in the amount of fecal nitrogen, it is evident that this retention of nitrogen must have some tissue-building significance. There is also a decline in urinary sodium, associated with a somewhat smaller decline in urinary chloride, a decline in urinary potassium and in total urinary volume. The evident end result of this is in water retention and a general protein anabolism, noticeable in the genital tissue, but more objectivized in the soma, with resultant increased growth and muscle hypertrophy.

In other clinical experiments it has been found that testosterone propionate and methyl testosterone exercised similar effects.[5] The only exception appeared to be that some observers found that methyl testos-

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From the University of Southern California Medical School and the Los Angeles County General Hospital.

terone tended to promote hypercreatinuria whereas propionate decreased it.[4] It is now felt that the fundamental effects are the same. The apparent discrepancy in creatine metabolism is merely ascribable to the fact that in the case of methyl testosterone administration the nitrogen retention is so profound as to cause a spilling over of creatine. In comparing the clinical effects of methyl testosterone with the testosterone propionate, no significant differences could be observed in the prematures in our series. The intramuscular administration perhaps did offer advantages over the oral route in accuracy of dosage, but the ease of administration of methyl testosterone in propylene glycol and the freedom from the infection hazard are perhaps more worthy of consideration.

Daily observations for any of the previously mentioned signs of virilism revealed no significant difference between the groups. Our follow-up examinations during the first year continued to support these findings. Following prolonged and injudicious treatment with testosterone in some adolescent and adult females a lowering of the voice has been found.[2] We watched for such an untoward effect in the infants both during the administration period and throughout the first year following treatment but no abnormalities in cry could be detected. Roentgenograms of the long bones were taken at the beginning of the series and repeated at the end of the year. There was no difference in bone age between the controls and the treated infants, but in general all infants showed that slight delay in osseous development characteristic of prematures.

SUMMARY

Seventy-four premature infants, of both sexes, weighing under 2000 grams at birth were given either oral methyl testosterone 5 mg. daily, or testosterone propionate 4 mg. daily parenterally. A similar untreated group was observed as controls. A distinct shortening in the time required to regain birth weight and in the time required to gain to 2500 grams was noted in both treated groups. In four sets of twins the smaller, treated infant showed increased somatic development over its larger untreated control sibling. No contraindications to the use of testosterone compounds were observed.

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QUESTIONS AND ANSWERS

Question: What about mortality rates of treated and untreated prematures?

DR. MARK: In our preliminary series we have not found any statistically significant differences between the mortality rates of the treated and the untreated premature infants. This is understandable as our treatment was begun at the end of 24 hours and it is during this time that the greatest mortality occurs in premature infants. However, Varden, who has done similar work in a San Bernardino hospital with premature infants, reports a lower mortality rate in those individuals treated.

Question: Regarding testosterone, and the interval you use—three weeks—have you any information on other intervals that might be used, and any information on catheterizations or prolonged administration?

DR. MARK: In this, the first series we have ever attempted, three weeks was chosen arbitrarily. It was believed that during this time a maximum physiological effect could be obtained with no possibility of any adverse effects due to prolonged treatment. Our follow-up study at the end of the first year supports this view. Experimental work shows that up to eight months of treatment with high doses has no effect on the epiphyseal centers.

Some Diagnostic and Therapeutic Techniques in Cystic Fibrosis of the Pancreas

GORDON E. GIBBS, Ph.D., M.D., *San Francisco*

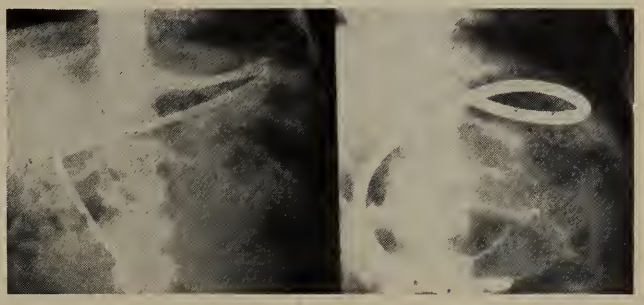
THE frequency of cystic fibrosis of the pancreas was appreciated only as recently as 1938.[2] The incidence has been estimated to be 1.7 per 1000 live births in New York City.[3] With the advent of penicillin some improvement in the prognosis has occurred.[11] Differentiation between cystic fibrosis of the pancreas and the various other entities of the celiac syndrome is often difficult, while the confidence resulting from a definite diagnosis favors adequate pursuance of the appropriate therapies.

The typical case of the fibrocystic disease is in an infant or child with history of chronic cough; soft, foul, bulky stools; retarded weight gain and growth, enlarged abdomen, poor musculature, and perhaps x-ray evidence of pulmonary inflammation and fibrosis. Microscopic examination of the stool for excess fat by sudan stain is a technique available to any office and is of great usefulness as a rough measure to aid in recognition of the celiac syndrome.[4]

In diagnosis of cystic fibrosis of the pancreas most reliance has been placed on the absence of trypsin from the duodenal fluid. In adults the most adequate technique of duodenal drainage has utilized the bi-lumen, gastro-duodenal tube. The gastric lumen permits withdrawal of the gastric fluid so that it does not contaminate the duodenal specimen. The need for such a technique, but the lack of successful application of it to infants, has been indicated by Andersen.[1]

In the present studies an attempt has been made to fill this need. Before a small double-lumen tube was devised, double drainage was accomplished by means of two separate tubes, one through each nostril (or one or both through the mouth in infants without teeth). Two tubes in place are shown in Figure 1A. This procedure was used in 30 tests and seemed to accomplish the objective of minimizing contamination of the duodenal sample by gastric contents. The duodenal tube was of 12 (French) diameter and had a gold tip. A 10 F or 12 F tube was used for the gastric drainage. The difficulties seemed to be due to the tendency of the two tubes to adhere so that introduction of the gastric tube after placement of the duodenal was somewhat more uncomfortable to the child, sometimes resulting in regurgitation of the duodenal tube into the stomach. Any separate adjustment of the tubes was difficult but the technique was usable and is desirable if a small bi-lumen tube is not available.

Figure 1B shows a bi-lumen tube, use of which has been apparently successful and thoroughly convenient in 31 attempts in patients ranging down to newborn size. This tubing also has 12 F outside diameter and is 120 cm. long.* It has two equal lumina, semicircular in cross section side by side. A gold tip of the same diameter (4 mm.) 15 mm. length, and 2.7 gm. weight is attached to the bottom.† Holes for the duodenal juice are immediately above this.



A B

Figure 1.—(A) X-ray showing two separate single-lumen tubes in place for separate drainage of gastric and duodenal fluids in a three-year-old child. (B) X-ray showing a bilumen tube in a 10-month-old infant. The duodenal tubes in the two films are of the same outside diameter (12 French).

Seventeen cm. higher, in the other lumen, are holes for gastric juice. This lumen is blocked below the gastric holes by a metal plug. Stubs of 15 gauge needles are tied into the upper end, through which aspiration is made alternately with syringes.

Entry of the tube into the duodenum is facilitated by placing the child on the right side. Directed by the weight of the tip, the lower perforations reach the pool of fluid in the pyloric corner of the stomach, as indicated by a steady drip or easy aspiration of fluid. Water is injected to maintain such a pool until the appearance of yellow juice usually heralds the passage of the tube into the duodenum. When clear, alkaline, yellow fluid is obtained from the lower lumen, while acid, turbid, white fluid comes simultaneously from the gastric, there can be little doubt that the tube is properly placed even without fluoroscopic verification, although the latter has always been used in the present study. In some cases, particularly in pancreatic deficiency, no duodenal fluid was obtained at first, and only at fluoroscopy was the tube discovered to be in the duodenum.

A good quantitative trypsin method is essential. In several debilitated infants without specific pancreatic deficiency the trypsin concentration was so low as to be undetectable by inexact office procedures, but high enough to rule out a typical case of cystic fibrosis of the pancreas.

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Senior Fellow in Pediatrics of the National Research Council, in Department of Pediatrics, University of California Medical School, San Francisco.

* The rubber tubing was made through the courtesy of Mr. Emil Davidson, Clay-Adams Company, New York City.

† The gold tip was made through the courtesy of Dr. W. A. Elsasser and Dr. W. L. Wylie, University of California College of Dentistry.

Values of 58 x 10^{-4} units of trypsin, 15 x 10^{-4} units lipase and 83 x 10^{-3} units amylase per cc. were obtained in the control child of whom the vitamin A curves are shown in Figure 2. This was a well-nourished two-year-old boy with occasional rectal prolapse. The infant in Figure 2 with pancreatic deficiency had zero values for trypsin, lipase and amylase. This infant had meconium ileus in the newborn period. She later developed a chronic cough. The duodenal drainage was done at the age of 8 weeks. (At this age a normal infant also shows no amylase.) The child representing celiac disease was 27 months old and had enzyme values of 21 x 10^{-4} U trypsin, 19 x 10^{-4} U lipase and 59 x 10^{-3} U amylase.

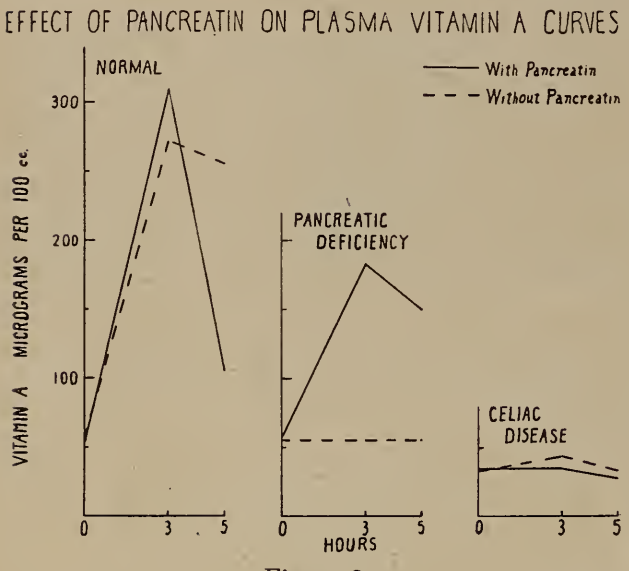


Figure 2

The rise in plasma vitamin A concentration which normally follows an oral test dose of vitamin A ester in fish oil does not appear in the celiac syndrome. Administration of pancreatin tends to correct the curve in pancreatic deficiency.[10] Curves from an infant with cystic fibrosis of the pancreas are presented in Figure 2. In this illustration the lack of effect of pancreatin on the normal curve of a normal child and on the flat curve of a child with celiac disease is also shown. These curves approximate the average obtained in 17 cases of cystic fibrosis of the pancreas, 10 cases of non-pancreatic celiac syndrome, and 12 controls. Use of this effect as a diagnostic measure has seemed a helpful adjunct to duodenal drainage. Its reliability is being further investigated.

Meanwhile the therapeutic implications of the effect deserve emphasis. The rise in vitamin A serves as an index of the effectiveness of pancreatin in restoring not only the digestion of vitamin A ester, but probably also of other foodstuffs. Inability to digest vitamin A ester may be circumvented by use of vitamin A alcohol.[10] Similarly, amino acids may be used to replace protein.[14] Prolonged use of an artificially hydrolysed, complete diet would, however, be difficult. The present data contribute to the assurance that relatively normal digestion can be achieved by the simple and practical expedient of adequate pancreatin therapy.[7] Corresponding data concerning the effect of pancreatin in protein digestion as indicated by blood amino acid concentrations has been presented by other workers.[16]

Dosage of 0.3 to 1.5 gm. of enteric-coated pancreatin granules following each meal has been used for routine therapy in the present series. 0.15 gm. pancreatin for each kg. body weight and 7000 units kg. vitamin A as halibut liver oil have been the test doses for the vitamin A curves. The tests were started before breakfast or the early morning formula and other vitamin concentrates were withheld.

Vitamin A curves with pancreatin in patients with pancreatic deficiency are also useful for comparison of the effectiveness of different pancreatin preparations and dosages.

Vitamin A has been determined by the Carr-Price reaction,[12§] pending acquisition of equipment for use of a capillary-blood method.[8]

In view of the fact that vitamin A levels of the plasma are depressed in both infection and impaired intestinal processes, determination of fasting vitamin A is of unique value in the follow-up of these cases.[13] In view of the possible effect of vitamin A deficiency to aggravate the pulmonary disease it seems advisable to keep the fasting vitamin A level within or above the normal range. This can be accomplished by high vitamin A dosage, pancreatin and antibiotics. We are using 15,000 to 50,000 USP units of vitamin A daily in most patients. As other indications of the status of the patients, the weight gain, leukocyte count, the penicillin sensitivity of the pulmonary flora and the interval history concerning cough, fever, and stools are also significant.

PENICILLIN AEROSOL

The terminal development in cystic fibrosis of the pancreas has been pulmonary infection. Benefit from use of penicillin has been dramatic. It seems obvious, however, that the best possible nutritional state, as maintained by vitamin A, pancreatin, etc., would

The studies here reported were done by the method of Anson, in which tyrosine from a hemoglobin substrate is determined with use of a photoelectric colorimeter.[5] The hemoglobin was prepared by dialysis of human over-age bank-blood. The more recent method using sulfanilamide azoprotein would probably also be satisfactory.[9] Amylase was determined by the volumetric hypoiodite method of Willstatter.[11] Lipase was determined by titration of the fatty acids liberated from 1.2 millimols benzyl butyrate in a bile-glycerol mixture.[6] One lipase unit liberates one milliequivalent of fatty acid per minute. Units are otherwise as defined in the references except that all digestions were done at 37.5°C. These three determinations could be completed within an hour. The tubes of juice were kept in an ice bath during collection and frozen if not immediately analyzed.‡

‡ I am indebted to Dr. I. L. Chaikoff and Dr. S. Chernick, Division of Physiology, University of California, for suggestions concerning the enzyme methods.

§ The method was standardized by use of the USP Vitamin A Reference Standard distributed by the Board of Trustees of the United States Pharmacopoeial Convention, 4738 Kingsessing Avenue, Philadelphia 43, Pa.

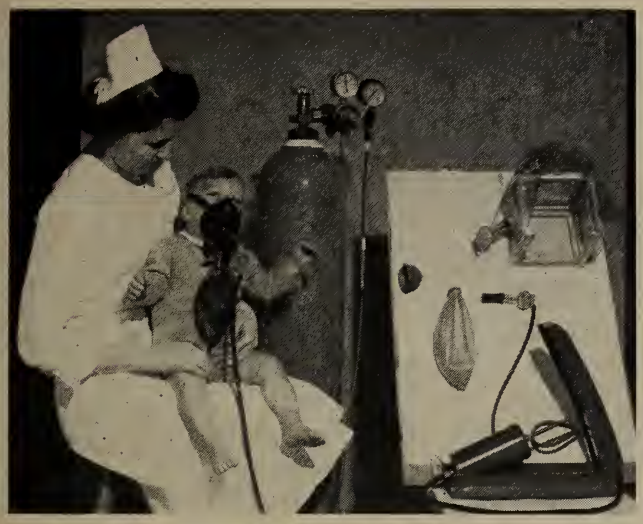


Figure 3.—Various equipment for penicillin aerosol administration.

be prerequisite to maximal success in penicillin therapy. Low fat diet and postural drainage are probably also of benefit.

The danger in patients receiving penicillin is the appearance of penicillin-resistant organisms. Such an outcome is believed to be facilitated by inadequate penicillin therapy. In our present program the periods (usually one to two weeks) of penicillin (25,000 to 50,000 units four times daily) alternate with periods without penicillin of a duration depending on the time of return of increased cough. Sulfonamides are usually used in prophylactic oral dosage during the periods when penicillin is not given. On the hospital ward, penicillin is given intramuscularly along with the aerosol inhalation. The program of use of aerosol alone represents a compromise with expediency which is practical in the home.

Some of the various arrangements for penicillin inhalation are illustrated in Figure 3. The oronasal B. L. B. mask is shown on the child.* The assemblies on the other side of the picture are alternative equipment. The box is for small infants. Some patients use oxygen tanks at home. Others have inexpensive automobile foot-pumps as illustrated. The foot-pump is especially satisfactory in case of a ten-year-old boy who coordinates his inhalations with strokes of the pump, and holds the nebulizer directly in his mouth. When a foot-pump is used it is advisable to insert a wad of gauze somewhere in the air line to catch any trace of oil, and the gauze should be changed from time to time. Difficulty has been encountered of some nebulizers being ineffectively constructed. Sometimes plugging of the small jet also occurs. Nebulizers must be tested occasionally by being held up to the light during use, for observation of the mist.

Twenty cases of cystic fibrosis of the pancreas have been studied at the University of California Hospital in the past year. Repeated weight records of 14 of the patients on essentially the regime recommended previously in this presentation, are at hand. Nine of the 14 have gained weight at a rate greater than the normal average for the age. Four others have also gained weight, but at a rate somewhat slower than the average. One, who was first seen after advanced pulmonary changes, lost weight over a six month period, was found to have a penicillin-resistant organism, responded poorly to streptomycin, and died.

* Size 4 B has been used, but is no longer available. We plan to use size 5 C instead. Mask and nebulizer assemblies are available through the University of California Pharmacy.

SUMMARY

Construction and use of a double-lumen gastroduodenal tube for duodenal drainage in infants is described.

The effect of pancreatin to raise the plasma vitamin A tolerance curve in pancreatic deficiency is illustrated and its therapeutic significance emphasized.

Equipment for administration of penicillin aerosol is illustrated and discussed.

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QUESTIONS AND ANSWERS

Question: Has any child with cystic fibrosis and lung changes ever reached puberty?

Dr. Gibbs: The oldest child that we have is ten years old, and judging by the way he is doing now, he should reach puberty. The oldest among Andersen's reported cases was 14½ years. I believe that there is a degree of mildness in cases, and we are at present investigating the probability that some fibrocystics may be mild enough so that they have survived into adulthood, although so far this has not been demonstrated.

Question: You stated the incidence of pancreatic fibrosis as being 1.7 per thousand. That seems a surprisingly high incidence to most of us. The question is: Does that not mean that a great many cases are being missed?

Dr. Gibbs: That is Dorothy Andersen's figure for New York City; we will have to take her word for it. This estimate seems more and more reasonable in view of the increasing number of cases that are being proven here—cases that in the past would have been fatal with some indefinite diagnosis.

Moderator: What is the adequate dosage of pancreatin?

Dr. Gibbs: We are feeling our way in that; it depends on the type of pancreatin that is used. The dosage that I am using therapeutically ranges from 0.3 to 1.5 grams of enteric-coated pancreatin granules after each meal. As judged by the effect on the vitamin A absorption curve, plain pancreatin should be given in twice the dosage.

Question: Have you employed liver extract and vitamin B parenterally to raise vitamin A absorption? (2) Have you performed the amino acid absorption curve as a substitute for duodenal assay as in New York City?

Dr. Gibbs: We use liver and vitamin B in celiac disease, and it seems very effective in certain cases. I doubt whether the amino acid absorption test is as reliable as duodenal assay. I have not used the amino acid test myself, but I mentioned the work of West and Wilson at Ann Arbor. They have, incidentally, obtained for amino acids essentially the same difference in curves with and without pancreatin, as I showed here for vitamin A. They determined the amino acids liberated from casein or gelatin.

Question: Does B_1 and liver injection still play an important part in the treatment of fibrocystic disease of pancreas?

Dr. Gibbs: That is an idea that should be played with. True celiac disease may be a sort of vitamin deficiency, something related to the vitamin B group, and it may possibly be precipitated by various types of intestinal disturbances including cystic fibrosis of the pancreas. I am waiting for a case of fibrocystic disease in which the nutrition and diarrhea do not respond to pancreatin, and will respond to vitamin B and liver, but have not found one yet.

Important Factors in the Diagnosis of Patent Ductus Arteriosus

Saul J. Robinson, M.D., *San Francisco*

With the advent of a highly successful surgical procedure to eliminate patent ductus arteriosus, diagnosis of the condition assumes more than academic importance. Unlike the operation for tetralogy of Fallot, the proper ligation or section of a patent ductus removes completely a pathological process and the final result is a normally functioning heart and great vessels. Thus far, nine years after the first successful correction of the defect, there has been no reason to feel other than that the operation is successful.

Everyone is familiar with the classical machinery murmur heard best in the second left interspace with a loud systolic and a softer diastolic component, which is characteristic of a patent ductus arteriosus. It is usually accompanied by a thrill. In the adult this characteristic murmur makes the diagnosis a comparatively simple matter when it is accompanied by the findings of a relatively wide difference between systolic and diastolic pressure particularly after exercise, by a systolic murmur heard over the apex, as well as by a characteristic roentgenographic pattern of the heart and an electrocardiogram which shows no right axis deviation. The criteria for diagnosis of patent ductus are thus established.

However, a careful study of the records of patients in whom patent ductus arteriosus was present although not discovered until operation or autopsy was done, indicates that there may be persons with this anomaly who do not present characteristic clinical evidence of it. Thus the to and fro murmur which is considered to be so intense, can actually vary from grade II to grade VI intensity. The diastolic component in turn may vary from an almost imperceptible grade I to grade V. There have been cases reported and confirmed by autopsy findings in which no murmur could be heard, presumably because of high pressure in the pulmonary artery.

In infancy and childhood, with which we are concerned, the common signs may be absent. The absence of the characteristic machinery murmur in infants and children renders the diagnosis of patent ductus arteriosus in this age period extremely difficult. In infancy the chest is so thin walled and the murmur which is limited to systole so widely transmitted, that the diagnosis cannot be made with certainty.

A sequence such as the following has been frequently encountered. A physician who has observed an infant from birth may note toward the end of the first year the development of a faint systolic murmur. At first the murmur may be indistinguishable from a functional murmur. Later it becomes so loud as to arouse suspicion of congenital malformation of the heart. Nevertheless, several years may elapse before the murmur develops the machinery quality which is so characteristic of patent ductus.

In recent years there have been added to the diagnostic aids two methods which utilize the x-ray. The first of these is the introduction of Diodrast, a radio-opaque dye, into the circulation, after which a series of roentgenograms is taken as the dye courses into and through the heart and great vessels. When the dye is introduced into the antecubital vein under pressure it may be found to remain longer in the chambers of the heart of a person having a patent ductus than it does in normal persons, presumably due to the passage of the dye from aorta into the pulmonary artery and back again through the lungs until it is finally diluted by the blood. However, it is a presumptive evidence and has not been found an infallible test.

A more successful modification has been the injection of the dye into the internal carotid artery, so that appearance of the dye almost simultaneously in the lungs and in the aorta may be looked upon as confirming evidence of a shunt between aorta and pulmonary artery.

Another method recently utilized is that of venous catheterization of the heart. A plastic catheter is threaded into a vein at the elbow, and successively into the right auricle, ventricle and pulmonary artery as well as into the pulmonary capillaries. This procedure gives valuable information when performed under fluoroscopic visualization; when the oxygen content of the blood in the heart, pulmonary artery and vena cava are measured and the blood pressures in the chambers of the heart and the great vessels are recorded. In the presence of a patent ductus arteriosus, the pressures in the right ventricle and pulmonary artery are equal. However, the oxygen saturation of the blood in the pulmonary artery is higher than that of the right ventricle, and the flow of the pulmonary capillaries exceeds that of the pulmonary artery.

It can be seen that if the pressure in the right ventricle exceeded that of the pulmonary artery, and the pulmonary blood flow were reduced, pulmonary stenosis must be suspected. The ligation or section of a ductus in such a case would destroy a valuable indirect source of blood to the lungs and might even result in death of the patient.

In conclusion it can be seen that the diagnosis of patent ductus arteriosus in the adults is in most cases not too difficult. There are, however, atypical

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cases which cannot always be differentiated by ordinary clinical means.

It must also be remembered that in infancy and early childhood the classical signs may be absent or incomplete and a definite diagnosis must in some instances be postponed until the child grows older, or the procedures outlined previously are utilized.

2107 Van Ness Avenue.

QUESTION AND ANSWER

Question: In the absence of any physical findings in infants and children, what are the indications for diodrast studies or venous catheterization?

DR. ROBINSON: In the absence of any physical signs or symptoms, I do not think you could even suspect heart disease —there would be no indication for diodrast.

Metatarsus Varus

FRANCES BAKER, M.D., *San Francisco*

METATARSUS varus, a common finding in infants, may be of very slight degree or it may be so marked as to make one consider pes equinovarus in the differential diagnosis. The condition is usually neglected unless the deformity is very striking, as there is a tendency for the foot to straighten, thus giving a more normal external appearance. Apparently the foot can appear quite normal even to careful examination until the child starts weight-bearing. Then a definite varus of the forefoot presents itself, usually with over-activity of the abductor hallucis muscle, so that the first toe in particular swings into medial position, with the inturn of the entire forefoot notably increased in comparison with the resting position.

Perhaps the lack of attention to this condition lies in the fact that the literature contains reports stating that normal alignment is reached by the end of the first year.[5] In attempting to explain the cause of foot strain in adults and to understand why one individual might suffer from painful feet with or without such extrinsic evidences as corns, calluses, bunions, clawing, inversions or eversions, muscular spasm, and increasing loss of flexibility, while others can wear any type of shoe without discomfort, we became more interested in deviations from normal in children's feet. By careful roentgen examination of adult feet, we can rule out such congenital abnormalities as accessory scaphoids, coalitions, or specific disease which may be found in a small percentage of patients. However, in most instances, when dealing with the chronically painful foot, we can find variations in the forefoot consistent with failure of full evolutionary development.

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From the Department of Physical Medicine, University of California Hospital, San Francisco, California.

The human foot is probably derived from a primitive mammalian foot, retaining its primitiveness supposedly because of the terrestrial habits. Jones[1] has stated the opinion that such a foot belongs to the primitive members of the primate stem, the stem from which man and the other existing members of the primates branched apart and went their separate ways at a very early stage. With the orthograde posture the feet were forced to take on the weight of the body.[2] This demanded an increase in the tarsus both in weight and in size, while the metatarsals and phalanges shortened. The opposing first toe came to lie beside the second. The changes, therefore, are (1) a progressive reduction of the anterior section (metatarsophalanges) and an increase in the posterior section (tarsus); (2) a change in the relative length of the digits, especially a reduction of the dominant third and an increase in the size of the first; (3) a gradual decrease in the abduction of the first and incorporation into the main structure of the foot; (4) a downward and backward extension of the os calcis to form a true heel and hence the appearance of the true arch; (5) a notable increase in the rigidity of the foot to fit it for its new purpose.

Therefore, in the normal foot which has developed completely according to evolutionary plan, Morton[4] has shown that the weight of the body is borne by the heel and the metatarsal heads. The static stresses are borne by the rigid framework of the foot, which is made up of bones and ligaments, while the muscles supply the kinetic power, and aside from keeping the body in balance, act only during locomotion. The weight of the body on the two feet can be divided into 24 units, each foot supporting 12 units. These are equally divided between the os calcis posteriorly and the metatarsal heads anteriorly. The wide first metatarsal head

rests on two sesamoid bones supporting one unit, thus making six points of contact with the ground. The foot then represents a triangle with its apex at the os calcis and the opposite side formed by the metatarsal heads. A line drawn from the os calcis should pass between the second and third metatarsal bones in erect standing, thus dividing equally the weight-bearing areas. In running, the full weight of the body will be thrust upon the metatarsal head of one foot (24 units), half of this being thrust upon the first metatarsal head alone. Then a line from the os calcis falls between the first and second metatarsals.

The weight of the body is transmitted through the astragalus (talus) to the os calcis, which forms a table upon which it rests. The bones of the mid-tarsal region represent a dome-shaped transverse arching, increasing the structural strength for forces applied vertically and converging the stresses toward the separate metatarsals, which are arched proximally but flattened distally so that their heads lie in a single plane.

The first metatarsal then is of particular importance to the internal mechanism of the foot: (1) It supports the medial side of the foot and prevents depression of the sustentaculum tali, thus preventing pronation. (2) It supports a major share of static stresses in locomotion. (3) It gives support to the astragalus, which is the center from which static stresses are distributed.

Any failure of normal evolutionary development, then, which interferes with the stability of the first metatarsal or changes the balance of weight-bearing so that the foot cannot conform to shoes or to long standing on hard surfaces is a potential cause for strain.

Barring severe trauma, paralyses, infections, etc., true foot strain can be attributed to certain deviations from the so-called normal foot which are inherited and represent a failure of full evolutionary development. Morton has defined certain anatomic variations which lead to definite strain: (1) a short first metatarsal, or (2) posteriorly placed sesamoids under the first metatarsal, and (3) hypermobility of the first metatarsal segments (including the first cuneiform bone which moves with the metatarsal). The short heel cord is considered as an extrinsic factor. He does not mention the metatarsus primus varus which is seen so frequently, but it does belong under the heading of "hypermobility of the first metatarsal segment." It has been discussed by many authors. Lapidus[3] described this condition as a primary cause of hallux valgus, since a large degree of angulation (10 to 19 degrees) exists between the first and second metatarsals with the first metatarsal in abduction.

In addition, I wish to add still another factor closely related to these as a cause of strain, namely, metatarsus varus, or a varus of the entire forefoot. This condition does persist into adulthood and can be easily demonstrated roentgenologically. Except by careful x-ray examination, it is difficult to recognize even when it is suspected, because the angle between the first and second metatarsals is normal since the entire forefoot is in varus and sufficient adjustment takes place in the tarsus to give a fairly straight medial line to the foot. We find, then, that in a large percentage of cases of foot strain in adults, the intrinsic causes are: (1) short first metatarsal; or posteriorly placed sesamoids under the first metatarsal; or hypermobility of the first metatarsal segment; (2) metatarsus varus, with or without metatarsus primus varus; and (3) the very important extrinsic factor—short heel cord. If individuals having feet of this type were not forced to wear shoes never designed for them, or to walk on hard surfaces which give no flexible support to the first metatarsal, then this deviation from the so-called normal would have little or no importance as these are fundamentally strong feet, failing only of full evolutionary development. The abnormalities are of course familial.

Recognizing that metatarsus varus does not disappear in childhood but persists in the adult foot, the question arises as to what correction should be attempted in infants. The amount of metatarsus varus in babies varies tremendously. Two infants in a series observed by the author gave the appearance of having clubbed feet, showing not only a pronounced varus deformity but the inversion of the tarsus and the short heel cords as well. The ease with which the last two elements were corrected with casts seemed enough to rule out true club-foot, but the varus deformity in one child has remained to a considerable degree; the feet of the other child show good correction at two years of age but the child is still wearing corrective shoes. The correction of the feet of the first child should have been much better had not an attempt been made to use leather molds after casting for only one month.

Pediatricians are realizing that routine development does not overcome the varus deformity but rather that it deserves special consideration. In spite of this, frequently babies with the deformity are not referred for orthopedic consultation until they begin to walk. Certain pediatricians who have been particularly alert to this condition, and who ordinarily refer patients for early care, have stated that the feet of those whom they referred late, appeared normal until weight-bearing began. Usually, the condition can be recognized immediately after delivery, and treatment should be started within the first two to three weeks. This simplifies the care as the child is ready for shoes by the time it is ready to walk, and it does not have to be constrained by casts with all the attending increase in care after walking is begun.

The author has placed casts on 32 of 60 babies observed for metatarsus varus and improvement has resulted. If it is decided that a correction should be forced, then casts are necessary, as no other simple support, such as a leather mold, will produce a shift in the forefoot. Casting is started at as early an age as possible and carried on for at least four or

five months. The casts are applied one week and wedged open on the medial side at the tarso-metatarsal junction the next week. They are changed completely every two weeks. Inasmuch as this condition is an inherited characteristic, the growth factor has to be considered, and, though the varus deformity can be corrected, if a wide angle is present between the first and second metatarsals this tends to persist.

When the condition is severe, there is often a tight medial band of soft tissue which is hard to stretch. When the varus is marked, and particularly when this medial band is present, casts should be used until appropriate shoes can be fitted. Although the first metatarsal may not entirely lose its broad angle with the second, the whole forefoot will be brought into better line with the tarsus and the ratio of weight-bearing improved. This in itself will permit the wearing of a more usual shoe. After the casts are removed, as the child is beginning to walk, shoes can be fitted to the opposite foot. Later the pronator type of shoe can be used or shoes of good quality can have a 1/8 to 3/8-inch lift on the lateral part of the sole and medial portion of the heel to thrust the forefoot into line with the tarsus. It is particularly important that the shoes be closely and accurately fitted. They should be worn at night as well as during the day.

When the varus deformity is of a moderate degree and passive correction is easily obtained, stretching by grasping the tarsus and moving the metatarsals lateralward at the tarsometatarsal junction should be done many times each day. When firm shoes can be fitted, they can be applied with the corrections described previously.

SUMMARY AND CONCLUSIONS

Metatarsus varus should receive more attention by pediatricians since it may not disappear but is frequently seen in adult feet and is a cause of strain and deformity. It can be present with metatarsus primus varus, with Morton's syndrome of short first metatarsal and hypermobility of the first metatarsal segment, or it can be present without evidence of these, in which case it is impossible to recognize without roentgenograms.

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What's New in the Treatment of Erythroblastosis

Herman Kirchdoerfer, M.D., *Pasadena*

THE Race-Fisher system of nomenclature of CDE-cde for the Rh-Hr system in the antigenic make-up simplifies the ever-increasing complexity of the problem of treating erythroblastosis and should be adopted universally. This system makes it possible to tell at first glance which persons will be sensitized, particularly in the rarer forms. The common single chromosome combinations are CDe, cde and cDE. If a woman with the genetic formula cde-cde (Rh-negative) is mated with a man whose genetic formula is CDe-CDe, (homozygous Rh-positive), the offspring will have the genetic formula of CDe-cde or always Rh-positive. If, however, this woman is mated with a man whose genetic formula is CDe-cde (a heterozygous Rh-positive), the offspring will have a 50-50 chance of being a cde-cde (Rh-negative). Formerly it was thought the Rh-negative lacked antigens, but we now know that they have three antigens known as c, d and e which are poor antigens and result in the rarer Hr factor. The anti-D serum has an 85 per cent specificity, the anti-c serum is important for the determination of heterozygosity, and anti-e serum for determining the 14 per cent who have a genetic formula, CDe-cDE.[6]

Until recently there was but one known method of treating erythroblastosis—multiple transfusions with Rh-negative blood, which was not adequate in all cases. Today a procedure known as exsanguination and replacement transfusion is available.

Exsanguination and replacement transfusion is indicated if there are severe signs and symptoms of erythroblastosis present at birth or if there is a family history indicative of chromosome incompatibility plus a strongly positive result of a Coombs' test,[5] conglutination test,[8] or gelatin test,[4] even though there is very little or no evidence of the disease at the time of birth. It remains to be seen whether exsanguination and replacement transfusion is advisable in cases in which there is strongly positive agglutination by one of the above methods but no history indicative of erythroblastosis and little or no evidence of the disease in the infant. There are several physicians in this country who feel that the procedure should be carried out in such circumstances, and yet in one of our recent cases only two transfusions were required. It must be emphasized that there are very mild cases of erythroblastosis fetalis in which the infant recovers without treatment, and some moderately severe cases in which multiple transfusions are effective.

The umbilical vein is used for transfusions done within 12 hours after delivery; for those carried out later, entry is made into the inferior vena cava by way of the great saphenous vein exposed in the upper thigh.[1] The use of the Diamond plastic catheter No. 18-19,[3] sterilized in Zephrin, for cannulizing these veins is the accepted procedure. Blood is withdrawn 20 cc. at a time and replaced with an equal amount of Rh-negative blood, the total of such exchanges varying from 250 to 500 cc. of blood, the amount depending usually on the severity of the disease. If anemia is present, 30 to 50 cc. more is given than is removed. Heparin, 10 mg. in normal saline, may be used as a rinse to keep the apparatus free of clots. As a final step 5 cc. of 10 per cent calcium gluconate is introduced through the cannula to counteract the excess citrate. It must be given well diluted, and better yet, in divided doses, to avoid heart block. Other procedures, such as withdrawal from the fontanel,[7] radial artery,[7] or femoral artery and introduction through the saphenous vein are used occasionally. Malony prefers to withdraw the blood from the umbilical vein and introduce the blood through the saphenous vein because in one case in which the blood was introduced through the umbilical vein, autopsy showed the mesenteric veins were thrombosed, resulting in a gangrenous bowel; and in another case free blood was found in the peritoneal cavity. Maintenance of oxygen supply and body temperature during the procedure is of utmost importance. Chemotherapy for four or five days thereafter is definitely indicated.

Induction of labor or Cesarean section for removal of the fetus prematurely in order to treat erythroblastosis should be used with reserve because the mortality rate from prematurity is greater than from the disease and actual benefit of the earlier treatment is very doubtful.

Beyond the measures now used, one other way of lowering the mortality rate from this disease is to have some program in each community whereby every pregnant woman may have the benefit of the Rh studies for a fixed price and those requiring further follow-up studies may have them without additional cost. In Pasadena such a program has proven very effective not only in lessening the financial burden of the Rh-negative mothers but in making it possible to alert the pediatrician for possible trouble.

The next step should be to prevent the development of this disease. We know that only one in every 25 of the Rh-negative wife and Rh-positive husband combinations have children with erythroblastosis and that in the presence of two antigens, antibodies will be produced for the stronger one. Therefore, it may be wise to give typhoid vaccine to Rh-negative sisters

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of Rh-negative mothers who have had infants with erythroblastosis, provided, of course, the blood of the sister's husband is such that erythroblastosis might be expected in the couple's offspring.

Bloxsom and Matthaei[2] have discovered a new factor, the anti-Rh antigen-antibody factor, which has been found to be present in high concentrations in Rh-negative mothers who, although having Rh-positive husbands, have normal offspring. As this factor has been found in Rh-negative male blood donors also, serum from these donors is being given to pregnant women in the hope of preventing or minimizing the disease in their children. Several other workers are using haptens, allergicil and normal saline for purposes of desensitization. Even if the anti-body titre can be reduced or the level maintained, it may not prove to be the answer, for frequently there is a marked discrepancy between the anti-body titre and the severity of the disease. It will be some time before work along this line can be fully evaluated and it will be interesting to follow the studies.

Another possibility for those having lost one or more infants and with husbands who are homozygous is artificial insemination with semen from an Rh-negative donor.

The publicity that has been given to the importance of erythroblastosis has caused undue alarm, particularly for young couples who have a hazardous Rh combination. It is the duty of physicians to explain to such persons that the disease occurs in only one infant in 25 whose parents have the combination, and that with present methods of treatment the mortality rate among infants who have the disease is about 10 per cent.

65 North Madison Avenue.

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QUESTIONS AND ANSWERS

Question: There is a question as to the indications for exsanguination transfusion. Let us take a child from the time of birth—whether or not he should have a transfusion.

DR. KIRCHDOERFER: If the child has all the signs and symptoms, particularly severe jaundice at birth, I think you go right ahead and assume he has erythroblastosis. If there is a family history of erythroblastosis and a positive reaction to agglutination tests or Coombs' test or other test, immediate exsanguination transfusion is probably indicated even though clinically the child does not seem to have the disease.

Question: Why give typhoid vaccine to mothers?

DR. KIRCHDOERFER: Weiner stated when you have two antigens present, the antibodies will be formed for the stronger antigens, and with that in mind it is believed that it disperses the others. That is just an idea that Weiner stated. I don't believe anybody ever tried it, or that there is anything on it—just a thought.

The Place of the Non-Operative Treatment in the Therapy of Perforated Peptic Ulcer

Roy Cohn, M.D., and Carleton Mathewson, Jr., M.D., *San Francisco*

THE treatment of patients with perforated peptic ulcer is a special problem in the emergency service of large city hospitals. Although surgical closure of the perforation is usually successful, the treatment of the patient with long-standing perforation or of one with generalized peritonitis is far from satisfactory. Recently[6] a report has been issued advocating the non-operative treatment of perforated ulcer. A series of cases has been studied to determine whether non-operative methods might have avoided any of the fatalities, and to ascertain the type of case suitable for non-operative care.

The present study is based upon 265 cases of perforated ulcer observed between July 1942 and July 1947. One hundred forty-eight were gastric ulcers and 117 duodenal ulcers. During this same period the medical services treated 244 patients with gastric and 529 with duodenal ulcers.

Butler[2] reported the experiences of this hospital in 251 cases in 1934. At that time the mortality rate was 24.5 per cent, which compared favorably with a review of 2,823 cases with a mortality rate of 29 per cent reported in the literature between 1896 and 1931. At that time, non-operative treatment was reserved in the San Francisco Hospital for those patients with perforated ulcers who were moribund from generalized peritonitis.

Many surgeons have pointed out the following factors which lead to an increase in the mortality rate in this disease: the duration of perforation before closure, the anatomical site of the ulcer, the volume and type of contents of the stomach at the time of perforation, the intake after perforation, the reaction of the peritoneum to infection, and the general condition of the patient at the time of perforation. The importance of the time factor is the simplest to demonstrate statistically. DeBakey[3] in 7,683 cases collected from the literature found the mortality rate in the first six-hour period to be 10.5 per cent, in the second six-hour period 21.4 per cent, in the third six-hour period 38.5 per cent, in the fourth six-hour period 62.4 per cent, and thereafter 61.5 per cent. These figures are in general agreement with other reports.[1,7] Taylor[6] has reported a series of 28 cases treated without operation. He argues against automatic surgical intervention in which no distinction is made between simple perforation and perforation in which the effects of peritonitis are the most disabling. Unfortunately, in only two of his patients was free air shown under the diaphragm so that from the abstracts presented in his paper one cannot be certain that these patients were not suffering from penetrating ulcers rather than from true perforations into the free peritoneal cavity.

From the Stanford University Surgical Service of the San Francisco Hospital, and the Department of Public Health, San Francisco.

During the period covered by the study, ten patients with proven perforated ulcers recovered without operation on the following regimen: constant gastric suction through a Levine tube, nothing by mouth, parenteral glucose solution and vitamins and sedation. Antibiotics were used in only three cases. Three patients refused operation, but in seven cases operation was not performed because of a serious complication, or because the patient appeared to be improving clinically. It is interesting that an ulcer in one patient (Case 4) perforated three times and the patient accepted operation for the second perforation only. In all cases except Case 6 free air was demonstrable by roentgenogram. In this patient an abscess was found walled off by the liver at the site of perforation. In the experience of this hospital, free air is present in 85 to 90 per cent of all cases of perforated ulcers. Its absence suggests that the perforation has been rapidly sealed off. If no free air is present in a patient who is clinically improving, we believe it safe to start out with the non-operative treatment.

RECOVERY WITHOUT OPERATION

1. A man of 63 complained of abdominal pain of 18 hours' duration. He had a four-year history of ulcer proven by roentgenograms. Examination showed abdominal tenderness and spasm. Leukocytes numbered 16,800. There was free air under the right diaphragm in "considerable" quantity. As the patient refused operation, he was treated with gastric suction and intravenous fluids. He was well when discharged 15 days after entry. The patient died in this hospital three years later from hemorrhage from the gastro-intestinal tract.

2. A man of 44 had acute abdominal pain of one hour's duration. He was said to have had a perforation of stomach ulcer eight years before, and was hospitalized but refused operation and recovered. Examination showed rigid tender abdomen with grunting respirations. A small amount of air was seen under the diaphragm by roentgenogram. The patient again refused operation and was treated by gastric suction, penicillin and intravenous fluids. Recovery was rapid and he was released from the hospital seven days later.

3. A man of 66 entered with complaint of acute onset of severe abdominal pain 12 hours previously. The patient had a long history of peptic ulcer proven by roentgenogram. He was operated on for perforation six years before. Examination showed a very sick man breathing with difficulty. Abdomen was spastic and tender and silent. Free air as well as pulmonary congestion at both bases was demonstrated by roentgenogram. Leukocytes numbered 20,300. He was treated with gastric suction, penicillin and intravenous fluids and slowly recovered. Signs of subdiaphragmatic abscess developed including neighboring fluid in the right chest. Both slowly absorbed and the patient was discharged well 34 days after entry.

4. A man of 41 entered 14 hours after the onset of acute abdominal pain. Examination showed tenderness in the abdomen and free air was shown under the right diaphragm by roentgenogram. Leukocytes numbered 22,000. The patient refused operation and was treated by gastric suction and intravenous fluids. He was discharged well 14 days later. The

patient reentered 19 months later. He had been operated upon for perforated ulcer in another hospital eight months previously. Again on entry to the San Francisco Hospital signs of peritonitis with free air under the diaphragm were found. The patient again refused operation and recovered sufficiently to be released one week later.

At a third and fourth entry four years later, he had no further perforations but was still suffering from ulcer pain.

5. A man of 53 entered 12 hours after the onset of acute abdominal pain. Abdominal examination showed tenderness in the upper quadrants only. Temperature was 101° F. Leukocytes numbered 17,000. Free air under the diaphragm was shown by roentgenogram. The chest was clear. The patient refused operation and was treated by gastric suction and intravenous fluids. He recovered rapidly and was released five days later.

6. A man of 57 entered five days after the onset of acute abdominal pain. He had a long history of ulcer. The patient was studied carefully and a diagnosis of duodenal ulcer made. No free air was noted. Thirteen days after entry, laparotomy was performed. A small abscess was found where a duodenal ulcer had perforated and had been walled off by the liver. Gastric resection was performed. Convalescence was uneventful.

7. A man of 38 entered with complaint of pain in the abdomen, nausea and vomiting associated with fever and weakness of two weeks' duration. He was said to have had tarry stools just before entry. Examination showed a sick man with a tender distended abdomen. Hemoglobin was 42 per cent and leukocytes numbered 16,000. Flat roentgenogram showed free air under the right diaphragm. With supportive therapy including gastric suction, intravenous fluids, transfusions and sulfadiazine, the patient slowly improved.

Twenty days after entry, a right subphrenic abscess was drained. The patient slowly recovered. Gastro-intestinal studies 41 days after entry demonstrated a large penetrating ulcer on the superior margin of the duodenum.

8. A man of 52 entered 42 hours after the onset of acute abdominal pain. The patient had had a perforated ulcer closed by operation at another hospital two months before the present episode. Examination showed the patient to be resting comfortably. The abdomen was tender throughout but no spasm was found. Peristalsis was hypoactive. Leukocytes numbered 15,000. The urine was normal. A flat roentgenogram showed elevated leaf of right diaphragm and wide separation of the loops of small bowel, suggestive of fluid, but no free intraperitoneal air.

The patient was treated with gastric suction, intravenous fluids and general supportive therapy with improvement. Gastro-intestinal studies, 14 days later, showed a duodenal ulcer from which a thin track of barium was seen to leak cephalad.

9. A man of 55 entered with acute abdominal pain and vomiting for the preceding 48 hours. Examination showed a distended silent tender abdomen. Leukocytes numbered 20,000. A flat roentgenogram showed "considerable" subdiaphragmatic air on both sides as well as gas in the small bowel. The patient was treated with gastric suction, penicillin, intravenous fluids and other supportive measures. He rapidly recovered and was discharged 13 days after entry. The patient was seen again seven months later for a minor fracture. He had no further gastro-intestinal symptoms. Gastro-intestinal studies showed "Spastic duodenal bulb, probably with duodenal ulcer."

10. A man of 56 with moderately extensive pulmonary tuberculosis entered 26 hours after the onset of acute abdominal pain. Examination showed tenderness and spasm in the upper belly. Abdomen was silent. Leukocytes numbered 30,000. Free air was noted under the right leaf of the diaphragm. Non-operative treatment was undertaken as symptoms and signs seemed to be subsiding. The patient recovered satisfactorily and gastro-intestinal studies three weeks later showed a penetrating duodenal ulcer. The patient had a thoracoplasty four years later, at which time he had no further gastro-intestinal complaints.

The patients in the following three cases (11, 12 and 13), although operated upon, would have recovered without operation, as the perforation was sealed. In none of these cases was free air noted by roentgenogram.

11. A man of 56 entered with a five-day story of abdominal pain. The onset was followed by persistent vomiting and intermittent hiccough. The patient had previous entries for luetic heart disease and cirrhosis of the liver. Examination showed the patient to be acutely ill. Abdomen was distended and tender especially in the right lower quadrant. Leukocytes numbered 18,200. A roentgenogram showed no free air but considerable gas in the small bowel. Operation was planned through a McBurney incision. The appendix was normal but purulent fluid present and a mass was seen in the right upper quadrant. The McBurney incision was closed and a right rectus incision made. A large mass of omentum as well as indurated colon were plastered to the duodenum. It was considered that this was a sealed duodenal ulcer so nothing further was done. The patient was treated with gastric suction, penicillin and intravenous fluids. He recovered satisfactorily. Two subsequent hospital entries have been made for heart disease.

12. A man of 61 entered ten hours after the onset of abdominal pain. The patient was doing heavy work when he was suddenly struck by pain in the left upper quadrant and when seen at another hospital was said to be in mild shock. At that hospital, a history of alcoholism and chronic stomach trouble was obtained. This the patient denied on entry to the San Francisco Hospital. Examination on entry showed no evidence of shock. Pain and tenderness were limited to the epigastrium. The patient had a fever. Leukocytes numbered 16,200. No free air was noted by roentgenogram; the diagnosis was in doubt. Some examiners considered perforated ulcer, others ruptured spleen, pancreatitis. Treated with gastric suction, penicillin and intravenous fluids, the patient improved. Gastro-intestinal studies 13 days later showed a large gastric ulcer on the lesser curvature, posterior wall. One month after the perforation, the patient had a gastric resection for a large gastric ulcer which had perforated into the undersurface of the liver.

13. A woman of 37 entered two hours after the onset of acute abdominal pain. The patient had a long history of duodenal ulcer which had been demonstrated by roentgenogram at another hospital. Examination showed a tender abdomen, not board-like in character. Peristalsis was active. Leukocytes numbered 16,000. No free air was seen by roentgenogram. With nasal suction and intravenous fluids, the patient improved over the course of the next few hours.

The abdomen was opened about eight hours later. A large firm anterior indurated prepyloric ulcer was found with a tiny perforation in its center. This had been sealed over with fibrin. Air and fluid could not be forced out of the hole. Attempts to close over the area so narrowed the pylorus that a gastric resection was done. The patient recovered satisfactorily and was discharged 15 days later.

Occasionally a large amount of free air may be found with evidence of peritonitis and yet careful search will fail to reveal the site of the perforation.

14. A man of 69 entered 38 hours after the onset of acute abdominal pain. The patient was known to have had peptic ulcers for 16 years prior to entry. He had been treated with Sippy powders and diet. On entry examination, he appeared acutely ill. Abdomen showed signs of generalized peritonitis.

Temperature was 105° F. Leukocytes numbered 11,400. Flat roentgenogram showed large amounts of air under both diaphragms. The abdomen was opened through a right rectus incision with ether anesthesia. A large amount of free fluid containing fibrin was found. Peritonitis was generalized. No source of the air could be found after careful and prolonged inspection of the abdominal viscera and the abdomen was closed. Culture of the peritoneal fluid showed a non-hemolytic streptococcus and an occasional Gram-rod.

After a stormy course, the patient recovered. A histamine test meal showed a high acid content. Gastro-intestinal studies and barium enema demonstrated no lesion.

The patient had another entry one year later at which time he had had no further gastro-intestinal symptoms.

DEATHS WITHOUT OPERATION

Fifteen patients died from perforated ulcers in whom no operation was performed because the patients were moribund on entry.

15. A woman of 47 entered with a complaint of four days of acute abdominal pain. Examination showed an obese woman moribund and in shock. The patient died shortly after entry. Autopsy showed a perforated ulcer with generalized peritonitis.

16. A man of 62 entered with acute abdominal pain of five days' duration. Examination showed a very ill man breathing with considerable difficulty. There were signs of pneumonia in the chest. The abdomen was silent and distended. Free air was seen by roentgenogram under both diaphragms. Leukocytes numbered 9,950. In spite of penicillin, oxygen, gastric suction and supportive therapy, the patient died two days after entry. Autopsy showed a perforated ulcer with generalized peritonitis.

17. A man of 46 entered with a three-day story of acute abdominal pain. He had been drinking heavily for some time before the onset of the pain and continued to do so afterward. Examination showed a sick man with obvious generalized peritonitis. Free air was seen under the diaphragms by roentgenogram. Leukocytes numbered 13,000. The patient was started on gastric suction and supportive therapy but died a few hours after entry. Autopsy showed a perforated gastric ulcer with generalized peritonitis.

18. A man of 70 entered two or three days after the onset of acute abdominal pain. He had a seven-year history of indigestion. Examination showed an old man in shock with signs of generalized peritonitis. Free air was seen under the diaphragms by roentgenogram. Leukocytes numbered 5,700. The patient died 12 hours after entry. Autopsy showed a perforated duodenal ulcer with generalized peritonitis.

19. A man of 45 entered with a 12-hour story of acute abdominal pain. The story was vague as the patient had been drinking heavily. Examination showed a very sick man in moderate shock with a board-like silent tender abdomen. Leukocytes numbered 7,000. Free air was seen under both diaphragms by roentgenogram. The patient died three hours after entry. Autopsy showed a perforated gastric ulcer with generalized peritonitis.

20. A man of 78 entered in such poor general condition that no history was obtainable. Examination showed him to be in shock and to have a rigid tender spastic abdomen. He was anemic. Erythrocytes numbered 2 million and leukocytes 32,800. Free air was seen under the right diaphragm by roentgenogram. In spite of supportive therapy, the patient died three days after entry. There was no autopsy.

21. A man of 57 entered 18 hours after the onset of acute abdominal pain. Examination showed a very sick, cyanotic, obese male in shock with the abdominal signs of generalized peritonitis. Leukocytes numbered 3,150. Diagnosis of mesenteric thrombosis was made. The patient died in 24 hours in spite of intensive supportive therapy. Autopsy showed a perforated duodenal ulcer with generalized peritonitis.

22. A man of 72 entered with a history of 16 days of vomiting, chest pain and shortness of breath. Examination showed a sick old man with silent distended tender abdomen. Flat roentgenogram showed free air and fluid under the right diaphragm. Leukocytes numbered 4,300. The patient refused operation and he died 24 hours later. Autopsy showed a ruptured gastric ulcer with generalized peritonitis, mitral stenosis and insufficiency, and cardiac failure.

23. A woman of 70 entered with a four-day story of acute abdominal pain and vomiting. The patient had a 20-year history of epigastric distress after eating. Examination showed an obese old woman who appeared moderately ill. Abdomen was tympanitic, tender and distended. Free air was demonstrated under the left diaphragm by roentgenogram. Leukocytes numbered 10,300. In spite of transfusion, intravenous fluids and gastric suction, the patient died four days after entry. Autopsy showed a perforated ulcer at the pylorus with generalized peritonitis.

24. A man of 63 entered 24 hours after the onset of acute abdominal pain. The patient was extremely ill and in mild shock. Examination showed signs of generalized peritonitis. Leukocytes numbered 15,000. Free subdiaphragmatic air was seen by roentgenogram. The patient died seven hours after entry. Autopsy showed a perforated ulcer with generalized peritonitis.

25. A man of 63 entered with a three-month history of abdominal pain after eating. Examination was not remarkable. At 3:30 the morning after entry, the patient complained of severe abdominal pain. Examination at this time by the medical house officer showed peristalsis present and no localizing abdominal signs. An enema was given. Examination was made by the surgical house officer a few hours later. He likewise believed the patient had a penetrating ulcer. The patient died a few hours later, two days after entry. Autopsy showed a generalized peritonitis from perforation of a gastric ulcer.

26. A man of 75 was brought in moribund and died a few minutes later. Autopsy showed a perforated duodenal ulcer with generalized peritonitis.

27. A woman of 47 entered four days after the onset of acute abdominal pain. Examination showed an obese female in shock. The patient died a few minutes after entry. Autopsy showed a perforated peptic ulcer with peritonitis.

28. A man of 58 entered with a 48-hour story of acute abdominal pain, vomiting and collapse. He had a 15-year history of peptic ulcer proven by roentgenogram. Examination showed a very sick man with signs of generalized peritonitis. Leukocytes numbered 2,500. Free air was seen under the diaphragms by roentgenogram. During the next 24-hour period he slipped further into shock in spite of supportive treatment and died. Autopsy showed a perforated gastric ulcer with generalized peritonitis.

29. A man of 49 entered with a complaint of sudden epigastric pain of three days' duration. He had a two-year history of epigastric distress relieved by soda. Examination showed an obese man in mild shock. The abdomen was silent, tender and spastic. Leukocytes numbered 20,000. Free air was seen beneath both diaphragms by roentgenogram. An ether anesthetic was started but the patient suddenly went into collapse, pulse became extremely rapid, cyanosis marked. Anesthesia was stopped and oxygen and transfusion were started. Shortly thereafter, the patient died. Autopsy revealed a perforated ulcer at the pylorus with no attempt at sealing. There was a generalized peritonitis.

The deaths from perforation following surgical closure were studied to see if any of these patients might have been saved had they been treated with-

out operation. There were 17 cases in this group. It is possible that Cases 33, 39, 45 and 46 might have survived without operation. These were older patients with perforations in the third group in DeBakey's classification. They were all chronically sick before the perforation occurred so that the risk of operation was correspondingly larger.

DEATHS FOLLOWING OPERATION

30. A man of 54 entered two hours after the onset of acute abdominal pain. He had a long history of indigestion. Examination showed an acutely ill man with a board-like tender silent abdomen. Leukocytes numbered 20,000. Flat roentgenogram showed free air under the right diaphragm and increased density in the right lower lobe.

The abdomen was opened through an upper right paramedian incision, using ether anesthesia. An 8 mm. perforation was found and closed. Six hundred cubic centimeters of peritoneal fluid were aspirated, cultures of which showed no growth after 72 hours. The patient did very poorly. The signs of peritonitis and obstruction supervened and he died 11 days after entry.

31. A man of 44 entered with an 18-hour story of acute abdominal pain. He had a five-year history of indigestion and epigastric distress. Examination showed a very sick patient with a distended silent tender abdomen. Leukocytes numbered 16,500. Free air under the diaphragms was seen by roentgenogram.

The patient was prepared for operation with plasma and intravenous fluids. Then under ether anesthesia a right upper rectus incision was made. Five thousand cubic centimeters of bile-stained fluid was aspirated. A 6 mm. perforation in the anterior wall of the duodenum was closed. The patient recovered satisfactorily from the operation but wound infection, parotitis and atelectasis then developed and the patient died on the 16th day. Autopsy confirmed the diagnoses and revealed a left pleural effusion.

32. A man of 68 entered 19 hours after the onset of acute abdominal pain. The patient had a long history of indigestion, tarry stools and alcoholism. Examination showed a very sick old man in shock. Abdomen was rigid and silent. Blood pressure was 65 mm. of mercury systolic, 0 diastolic. A large amount of free air was seen under both diaphragms by roentgenogram. Leukocytes numbered 8,500.

Prior to operation, the patient was given 500 cc. of whole blood, 500 cc. of plasma and 1,0000 cc. of glucose in saline without much improvement. Under ether anesthesia, the abdomen was opened and a large amount of purulent fluid aspirated. An 8 mm. perforation was found on the anterior wall of the stomach. This was sutured. After transfusion of 500 cc. of blood, the patient improved somewhat. With gastric suction, penicillin and intravenous fluids, the signs of peritonitis slowly subsided. But the patient began to fibrillate and passed decreasing amounts of urine. The nonprotein nitrogen slowly rose to 252 mg. per 100 cc. as the urinary output fell off. Fourteen days postoperatively, the patient began to secrete urine again but expired suddenly on the 17th postoperative day. No autopsy was obtained.

33. A man of 72 with a ten-year history of "stomach trouble" was admitted to the urological service because for 14 hours he had been unable to urinate. As most of the difficulties seemed to be associated with prostatic obstruction, he was treated for this lesion. Eighteen days after entry, a transurethral resection was done. Three days later abdominal distention, tenderness and spasticity developed. Flat roentgenogram showed no free air but cystograms were interpreted as showing a ruptured bladder. When a suprapubic cystostomy was performed, no rupture was found in the bladder but cloudy peritoneal exudate was seen coming from the upper abdomen. An upper abdominal incision was made and a large perforated gastric ulcer found after considerable difficulty. The surgeon was not sure that the patient did not have an old gastro-enterostomy with a perforated marginal ulcer. The patient was in very poor condition at the end of this procedure. In spite of transfusions, penicillin and other supportive therapy failed and the patient died nine days after operation. Autopsy showed multiple intraperitoneal abscesses. The sutured ulcer was 8 cm. from the cardia on the greater curvature. There was also a moderately severe cystitis and pyelonephritis as well as bronchopneumonia.

34. A man of 57 entered with acute abdominal pain which had begun four or five days before. The pain had been constant since, associated with vomiting, and radiation to the shoulders. The patient had been drinking and he was known to have had "stomach trouble" for many years. Examination showed moderate distention and tenderness throughout the abdomen. A large amount of free subdiaphragmatic air was seen on the flat roentgenogram. Leukocytes numbered 9,600. A laparotomy under cyclopropane revealed a perforation of the stomach on the lesser curvature, anterior surface, close to the esophagus. Postoperatively the patient developed signs of pneumonia and died on the eighth day. Autopsy showed the cause of death to be generalized peritonitis.

35. A woman of 47 entered with acute abdominal pain of nine hours' duration. Examination showed a rigid tender silent abdomen. Leukocytes numbered 9,000. Free air was seen under both diaphragms by roentgenogram. An operation under cyclopropane revealed a large amount of free fluid which cultured a non-hemolytic streptococcus. A 1 cm. perforation was found on the anterior surface of the stomach 2 cm. from the pylorus. This was sutured. In spite of penicillin, gastric suction and supportive therapy, the patient died on the second postoperative day. No autopsy was obtained.

36. A man of 47 entered 48 hours after the onset of acute abdominal pain. He had a 20-year history consistent with peptic ulcer. Examination showed the patient to be acutely ill but not in shock. There were the usual abdominal signs of generalized peritonitis. Leukocytes numbered 13,400. Free air was seen under the right diaphragm by roentgenogram. Operation under local anesthesia revealed turbid peritoneal fluid and a perforated gastric ulcer on the lesser curvature near the pylorus. This was closed. The patient became much sicker postoperatively, developing delirium tremens and bilateral pneumonia. He died six days after entry. No autopsy was obtained.

37. A man of 62 entered 30 minutes after the onset of acute abdominal pain. He had been treated in this hospital for the preceding two years for gastric ulcer. Examination showed an old man with a board-like tender silent abdomen. Leukocytes numbered 10,300. Free air was seen under both diaphragms by roentgenogram. Operation about five hours after perforation, using spinal anesthesia, revealed 600-800 cc. of peritoneal fluid containing food particles. The perforation which was on the lesser curvature of the stomach near the pylorus was sutured. The patient recovered satisfactorily and was discharged 18 days postoperatively. He reentered the hospital two weeks later complaining of abdominal pain, swollen joints, fever and diarrhea. The exact nature of the illness was not determined. One morning without warning he complained of severe abdominal pain, went into shock and died. Autopsy demonstrated that a residual liver abscess of long standing had suddenly ruptured into the free peritoneal cavity.

38. A man of 58 was brought into the urological ward in an alcoholic state by the police because of urinary incontinence. He was covered with filth and on the verge of delirium tremens. Six days after entry he complained of severe abdominal pain. Examination revealed a tender spastic abdomen. Considerable air was seen under both diaphragms by roentgenogram. The patient was operated upon under cyclopropane about eight hours later. Turbid fluid was encountered and then a large abscess cavity was entered completely surrounded by omentum. After this had been evacuated, a perforation was found in the duodenum. This was closed. The patient did not recover from the shock of the procedure and died 12 hours later. No autopsy was obtained.

39. A man of 69 entered 16 hours after the onset of acute abdominal pain. The patient stated he had been in poor health with abdominal pains for one year and had lost 25 to 30 pounds. Examination showed a sick old man with abdominal signs limited to the upper abdomen. Leukocytes numbered 28,000. Free air was seen under the right diaphragm by roentgenogram. Operation under cyclopropane revealed a perforated prepyloric ulcer. Postoperatively the patient developed bronchopneumonia, parotitis and died on the 14th day. Autopsy confirmed the clinical findings. The peritonitis had been adequately handled.

40. A man of 73 entered 18 hours after the onset of acute abdominal pain. He had a ten-year history of intermittent abdominal pain relieved by soda. Examination showed a sick old man with a rigid tender silent abdomen. Leukocytes numbered 6,650. Free air was seen under the diaphragms by roentgenogram. Operation under cyclopropane revealed a large amount of turbid fluid and 5 mm. perforation at the pylorus. The peritoneal fluid showed hemolytic streptococci and E. coli on culture. Postoperatively the patient had considerable urinary difficulty which necessitated constant drainage. Although his abdominal signs subsided, unilateral pneumonia developed, and in spite of supportive therapy he died on the 14th postoperative day. No autopsy was obtained.

41. A man of 67 entered 15 hours after the onset of acute abdominal pain. Examination showed tenderness and spasm in the right upper quadrant. No free air was seen by roentgenogram. Leukocytes numbered 13,700. Operation under local anesthesia with a diagnosis of acute cholecystitis revealed a large amount of free peritoneal fluid. A 4 mm. perforation was found in the anterior surface of the stomach 3 cm. from the pylorus. This was sutured. The patient died two days later. Autopsy showed generalized peritonitis, with smears showing numerous cocci. There was an acute ulcerative esophagitis present for which there was no explanation.

42. A man of 73 entered three hours after the onset of acute abdominal pain. The patient had a long history of stomach disturbances. He had also been under treatment for heart disease. Examination showed a sick old man with abdominal signs limited to the upper quadrant. There was fibrillation and ankle edema. Leukocytes numbered 13,000. Large amounts of free air were seen in the peritoneal cavity by roentgenogram. Operation under local anesthesia and ether revealed 2,200 cc. of turbid fluid in the abdomen and a large perforated anterior duodenal ulcer. The patient did very poorly postoperatively. Wound infection developed and was followed by evisceration, necessitating secondary suture. The patient died one month after operation.

43. A man of 42 entered seven hours after the onset of acute abdominal pain. On examination the patient did not appear particularly ill. The abdomen was tender throughout and silent, but only slightly distended. Leukocytes numbered 4,000. Free air was noted beneath both diaphragms. Under ether anesthesia the abdomen was opened and large quantities of turbid fluid aspirated. A 3 mm. perforation was found on the anterior wall of the stomach near the pylorus. This was sutured. The patient went into shock postoperatively and, in spite of transfusions, died. No autopsy was obtained.

44. A man of 65 entered eight hours after the onset of acute abdominal pain. The patient had been ill with chronic heart failure for two years, but had had no ulcer symptoms previous to a week before entry. Examination showed a thin old man with a rigid tender silent abdomen. Leukocytes numbered 17,000. Free air was seen under the right diaphragm by roentgenogram. Under local block anesthesia, an anterior gastric perforation, 3 mm. in diameter, was closed. There was very little fluid in the abdomen. Immediately postoperatively, the patient became extremely cyanotic and, in spite of oxygen therapy, died a few hours after operation. The cause of death was presumed to be heart failure. No autopsy was obtained.

45. A man of 57 entered 24 hours after the onset of acute abdominal pain. Language difficulty made the story unreliable. The patient had had a duodenal ulcer demonstrated by roentgenogram in this hospital. Examination showed that the patient did not appear severely ill. The abdomen was silent and tender but not spastic. Leukocytes numbered 4,050. Free air was demonstrated under the diaphragms by roentgenogram. Under cyclopropane anesthesia, a large amount of thin fluid containing fibrin was aspirated from the abdominal cavity. A prepyloric perforation was sutured. The patient's liver was enlarged and nodular. Two days postoperatively, the patient died.

Autopsy showed the peritoneal cavity to be clean and the ulcer well sutured. Death presumably was due to cirrhosis of the liver. A diagnosis of cirrhosis of the liver with ascites had been made also on the previous hospital entry. The patient had had a head injury just before the onset of symptoms of perforation, which, added to the language difficulty, confused the history.

46. A man of 58 entered 36 hours after onset of acute abdominal pain. The patient had a long history of stomach disorder for which he had had an operation ten years before (Billroth I). He also had active pulmonary tuberculosis for which he was undergoing treatment at the time of entry. Examination showed a sick man in mild shock with a silent tender abdomen. Leukocytes numbered 17,000. Free air was seen under the right diaphragm by roentgenogram. Operation, which was done under spinal anesthesia, after transfusion and 1,000 cc. of glucose, revealed a large amount of thin fluid in the abdomen. There was a marked amount of induration of the entire pyloric region of the stomach but only a tiny perforation. This was sutured. Postoperatively, although the perforation appeared to be handled satisfactorily, the patient became disoriented, attempted suicide. Extension of the pulmonary signs developed, the patient had a large hematemesis and died on the 19th postoperative day.

Autopsy confirmed the clinical findings and revealed the cause of death to be massive hemorrhage from an ulcer perforating into the head of the pancreas.

There were 32 deaths from all causes in this series of 265 cases of perforated ulcer, a mortality rate of 12 per cent. Since seventeen patients died following operation, the surgical mortality rate is 6.4 per cent. A similar mortality rate was reported by Graham[4] in a series of 125 cases in which operation was done. Graham emphasizes the preoperative preparation of patients and believes that all patients should be op-

erated upon. Of five patients who were not operated upon, all died.

If one is to pursue a delaying policy in the selected cases of perforated ulcer, careful clinical examination and re-examination must be employed. If the patient's condition becomes worse, after once having reached a level, one should operate at once, as in the following case:

47. A man of 54 entered two hours after the onset of acute abdominal pain. The patient had had symptoms suggestive of peptic ulcer for several months before entry. Symptoms had been worse the week before entry. Examination showed tenderness and spasm in the epigastrium. The patient had a slight fever. Leukocytes numbered 11,900. No free air was seen in the peritoneal cavity by roentgenogram.

The patient was observed the next few hours on the ward. Gastric suction was started and intravenous fluids were given. The tentative diagnosis was perforated ulcer which had sealed off. A few hours later the patient's temperature and pulse rose and reexamination showed increased abdominal signs. Operation was decided upon.

When the stomach was exposed, a considerable amount of fibrin was found on the anterior surface just proximal to the pylorus. A tiny perforation was seen in the middle of this fibrin plug. A moderate amount of free fluid was found in the peritoneal cavity which on culture showed only a yeast. The patient recovered satisfactorily. He died five years later from a gastric hemorrhage.

DISCUSSION

During the years from 1934 until 1948 the mortality rate from operations for acute perforation of peptic ulcer has been lowered in this hospital from 24.5 per cent to 6.5 per cent. This decrease is attributable mainly to a better trained house staff, a more general use of gastric suction, the use of antibiotics and chemotherapeutic agents and the careful preparation and selection of patients for operation.

In view of recent publications on the non-operative treatment of perforated peptic ulcers[5,6] an attempt has been made to analyze the deaths in this series to determine whether or not the outcome might have been altered by non-operative methods. Ten patients with proven perforations survived without operation while 15 died under similar management. Ten of the latter—they had been considered moribund at the time of entry—survived less than 24 hours. Of the remaining five, only one was considered for operation and he died following the administration of anesthetic. All 15 patients died of a generalized bacterial peritonitis. It is significant that of the ten patients who survived with non-operative treatment, four had previous perforations and the remaining six had long histories of ulcer symptoms. Although all of these patients had evidence of free air in the peritoneum, it is reasonable to assume that previous vaccination of the peritoneum and partial walling off of the peritoneal cavity with preformed adhesions were dominant factors in localizing the peritonitis and in facilitating recovery without operation. Three patients who were operated upon and found to have perforation sealed by a plastic exudate, survived without suture of the ulcer site.

It seems evident to us from these observations that the patient most likely to survive non-operative treatment is the patient who for one reason or another has peritoneal adhesions preventing general contamination of the peritoneal cavity following acute perforation. Such patients show clinical evidence of localized peritonitis and improve rapidly under observation. How one is to select such patients for conservative therapy is the problem.

In this study, 17 patients died following suture of the perforation. Of these, only four seem unwisely selected for operation. Possibly the course in these cases might have been altered by conservative management. However, this seems unlikely in view of a generalized peritonitis at the time of operation with no evidence of sealing of the ulcer.

The analysis of the deaths in this series seems to indicate that the patients least likely to survive an acute perforation are those who are suffering with an acute generalized bacterial peritonitis with an unsealed perforation whose general condition cannot be altered to permit operation. Only in exceptional circumstances do such patients recover on conservative management. On the other hand, patients who show no evidence of free air in the peritoneum, patients with previous perforations or a long-standing history of ulcer and localized peritonitis, may recover on conservative management. Non-operative treatment is indicated in such patients only when other considerations such as chronic alcoholism, pulmonary, renal or cardiac impairment contraindicate operation.

SUMMARY

1. Studies of 265 patients with perforated ulcer at the San Francisco Hospital reveal an overall mortality rate of 12 per cent with an operative mortality rate of 6.4 per cent.

2. Patients with perforated ulcer can survive without operation.

3. In the non-operative treatment of perforated ulcer, it would seem justifiable to delay operation in all those patients in whom peritonitis is apparently becoming localized and who seem to be improving clinically. One would be encouraged in this stand if no free air could be demonstrated in the peritoneal cavity by roentgenogram.

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Management of Acute Peritonitis

Clarence J. Berne, M.D., *Los Angeles*

ACUTE bacterial peritonitis has long maintained its position as one of the most dreaded of intra-abdominal lesions. In the past decade such important progress has been made in its therapeutic control that an integration of these developments may profitably be presented. In this discussion the assumed problem is the presence of an established, diffused, polymicrobic, enterogenous peritonitis. In general, acute peritonitis follows a pattern of three phases: an initial period of diffusion, lasting from a few hours to several days depending on its pathogenesis; a second period of established active peritonitis lasting seven to ten days; and, if recovery is to occur, a period of resolution. Residual abscess formation or mechanical intestinal obstruction may complicate this latter phase. Excepting complicating factors peculiar to the individual patient, the prognosis in acute peritonitis is dependent upon three factors: the lesion producing the peritoneal infection, the degree of sepsis, and the severity of the invariably associated, inhibitive type of intestinal obstruction.

One group of cases that can be used for measuring progress in the treatment of acute peritonitis is that of appendiceal origin. An excellent series for reference in this regard is that from the Cincinnati General Hospital, reported by Tashiro and Zinninger.[13] In the years 1915-1933, perforated appendicitis with peritonitis carried a mortality of 33.9 per cent. In the next five-year period (1934-1938, inclusive) this figure had been reduced to 17.2 per cent and in the five years 1939-1943 the rate had further declined to 13.8 per cent. The decline was attributable to improved surgical management of the individual cases, and to a vigorous lay educational campaign aimed at encouraging earlier medical attention and eliminating the use of cathartics. This latter approach is even today potentially the most effective means of controlling the mortality from peritonitis.

TREATMENT OF THE INDIVIDUAL CASE

After properly disposing of the problem of the primary lesion productive of acute peritonitis, the surgeon finds the subsequent phase of management determined by the existing peritonitis. In designing the regimen to be instituted, the three major elements of the peritonitis can be defined as follows: the systemic, the intestinal obstruction, and the septic factors.

SYSTEMIC DISTURBANCES

Perhaps the most promising future therapeutic possibilities in the sytemic phase of peritonitis are those indicated in the reports by Kay and Lockwood.[6,7] In their studies on dogs, the standard experimental situation was an appendiceal peritonitis produced by ligation of the base of the appendix and its mesentery, with a mortality of 41.7 per cent in a series of animals. In these animals, blood nonprotein nitrogen, total protein, chlorides, sodium and potassium levels were not significantly different in the survivors than in the animals that died. Blood taken during the crisis of peritonitis did not clot readily and when it did the thrombus was soft and non-retractile. In those instances of complete failure to clot the animals invariably died. There was spontaneous lysis of the clot within 48 hours in all animals that died, although some with this phenomenon did live. Associated with this increased proteolytic activity there was a prolongation of prothrombin time, and if this prolongation amounted to only a few seconds at the onset of the peritonitis the mortality was increased. If animals were fed trypsin preoperatively, the mortality was reduced to 6.6 per cent, by reason of the increased antiproteolytic activity of the serum of the treated animals. Because the proteolytic enzyme system of the serum is capable, unless inhibited, of quickly destroying the total fibrinogen of the body, the work of these investigators would indicate that disturbances of this system are potentially of great clinical importance in peritonitis.

In the hospital, active treatment of the systemic disturbances constitutes an essential phase of the management. The optimum position of the patient in bed is not yet agreed upon. The full Fowler's position has, however, been generally discarded as unphysiological, partly because of the manner in which it affects pulmonary and peripheral venous physiological processes. Further, the ability of Fowler's position to retard the development of upper abdominal abscess can be challenged. This challenge is based on the contention that the associated intestinal distention usually creates sufficient intra-abdominal pressure to exceed the effect of gravity and thereby neutralize the benefits of a semi-sitting position. It is our preference to have the bed flat, permitting the patient to roll, or be rolled, freely from side to side. This accomplishes, in principle, a horizontal axial circumrotation. Such a position, in conjunction with ankle exercises, qualitatively approximates many of the benefits of early ambulation. This alternate shifting of the dependent half of each lung to an opposite position in relation to the bronchial tree and to the heart, promotes bronchial and pulmonary venous drainage, as does the resultant full excursion of the diaphragm. If desired, the head end of the bed can be raised on blocks to improve vital capacity and secure the effect of gravity, but preserving freedom of mobility. An incidental beneficial effect may be that of shifting the kinked dilated loops of intestine, thereby promoting movement of fluid into the colon.

From the Department of Surgery of the Los Angeles County General Hospital and the University of Southern California School of Medicine.

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Loss of the function of alimentation has frequently cost the life of a patient in whom the peritoneal infection would have healed if healing had not been handicapped by this starvation and fluid deprivation. Parenteral alimentation is a practical problem today, with most of the needed materials available. Fat, the one major element not yet generally available for intravenous use, is physiologically the least important. The average patient with peritonitis possesses adequate fat depots for the duration of the disease. Sound management requires a careful daily prescription of calculated amounts of water, sodium chloride, glucose, amino acids and vitamins, with less accurate but equally important efforts to replace blood proteins and erythrocytes by transfusion of whole blood, aimed at maintenance of a normal blood volume.

In the average hospital, water balance is best maintained by study of the daily urine output. If urine specific gravity is over 1.015, an output of 1000 cc. is ordinarily adequate. The most difficult phase has to do with the dose of sodium, partly because our understanding of sodium need in general is in a state of revision, and partly because it is being recognized that sodium chloride retention occurs in peritonitis. A daily dose of 9-12 gm. of sodium chloride would seem to be the maximum advisable in the average case even with indwelling gastric suction, except for patients with perforated peptic ulcer, whose hyperchlorhydria conditions a precocious dechlorination. It appears that the usual error is to give too much sodium, especially in the older patients. One approach to the problem is to favor glucose in water, and to add sodium upon the appearance of diuresis. This is based upon the fact that the interstitial fluid pool of the body requires sodium to hold its water, and that diuresis is indicative of the dumping of water because of insufficient sodium to hold it in this pool. Such a diuresis, therefore, is evidence of sodium want. To build the pool volume back to normal requires both sodium chloride and water. Carbohydrate administration, as 5 or 10 per cent aqueous solution of glucose, spares protein, reduces ketosis, and reduces the caloric deficit. Too rapid administration results in glycosuria and diuresis. Ten per cent glucose solution is often preferable, given slowly the first half hour, and then given at a rate so that from 2 to 2½ hours is required for the administration of 1000 cc. The nitrogen deficiency in peritonitis can now be effectively influenced by the administration of 5 per cent amino acid solutions, preferably with 5 per cent glucose. Very special precautions are required to avoid reactions. A liter of this solution daily, with adequate complementary glucose, is a specific attack on the problem of negative nitrogen balance, most easily visualized by the fatty liver, with its multitude of attendant hepatic dysfunctions. In the vitamin phase of therapy, a daily parenteral dose of crude liver extract gives coverage of an extensive list of these elements. Thiamine, riboflavin, nicotinamide, and ascorbic acid are commonly considered to be desirable additions if excessive doses are avoided.

INTESTINAL OBSTRUCTION

In addition to the loss of nutritional intake, the patient with peritonitis is subjected to most of the disturbances of low simple intestinal obstruction, by reason of the inhibitive ileus. Among these disturbances the factor of distention usually is the most tangible at the bedside. In the experimental laboratory, distention has been proven to be an extremely important element in the pathologic changes of intestinal obstruction. Perhaps the most notable early investigation of the effects of distention was by Van Zwalenburg of Riverside.[14] Herrin and Meek[5] have shown that distention of the jejunum without obstruction of it will produce dechlorination, dehydration, and death almost as regularly as will obstruction of it. In treating distention the surgeon cannot control the hypersecretion and decreased absorption producing excessive intraluminal fluid. However, the increased intestinal volume is to a large degree dependent on the accumulation of gas. Because most intestinal gases do not exist in the atmosphere, they can be absorbed by the blood and be passed off by the lungs. Because the atmosphere is largely nitrogen, this particular gas cannot be disposed of in this way, and, in effect, swallowed air, largely nitrogen, becomes a foreign body in the intestinal tract. An indwelling gastric catheter, with suction, as first suggested by Ward of San Francisco,[15] will prevent this swallowed air from entering the intestinal tract.

Various devices to provide suction, and tube modifications to secure gastric, duodenal, jejunal or ileal levels of drainage have been developed for removing gas and accumulated secretions. These devices are of very great importance. Instead of waiting until distention develops, the surgeon should use gastric or duodenal suction as soon as a diagnosis of peritonitis is made. If distention of significant degree is present, intubation and suction may be required at lower intestinal levels. It should be indicated that when peritonitis heals, deflation will occur spontaneously. Distention should never be treated with peristaltic stimulants, which may be lethal.

All of the foregoing considerations focus on the treatment of the ileus by mechanical decompression of the orad segment of the gastro-intestinal tract, and attempt to emphasize the great value of such measures.

TREATMENT OF THE PERITONEAL INFECTION

Until recently, administration of Cl. Welchii antitoxin and the transfusion of blood from individuals convalescing from enterogenous peritonitis constituted the only direct therapeutic attack on the peritoneal infection. With the use of the sulfone compounds in peritonitis a decrease in the mortality rate was generally observed. Tashiro and Zinninger[13] reported a mortality of 11.3 per cent when these drugs were used systemically in general peritonitis, as compared with 18.8 per cent in a comparable group of patients who did not receive them.

The value of penicillin in acute appendiceal peritonitis was indicated in the report of Crile.[1] In his series of 50 cases from a Naval hospital, there was only one death and that was due to mesenteric thrombosis. These patients were treated with doses of 100,000 units of penicillin every two hours, and it was concluded that the resultant high concentrations were adequate to permit a positive effect on the coccal organisms in spite of the inhibiting effect of the penicillinase produced by the Escherichia coli. No comparable series in which streptomycin was used has been reported as yet.

In the laboratory field, using Gram-negative bacilli, it has been shown that an average lethal dose of their endotoxins could be raised two times if the animals were protected with crystalline penicillin, and eight times using mixed penicillin.[8] This endotoxin neutralizing effect, it should be emphasized, is independent of any bactericidal activity. Another significant observation regarding penicillin relates to bactericidal doses in vitro.[2] For a particular organism, gradually increasing concentrations determine "a maximally effective concentration which varies between two and ten times the 'sensitivity' level of the organism as ordinarily defined." Even a 20,000 fold increase does not intensify this effect, and, in not a few strains the level of activity is reduced by the higher concentrations. Up to the present time in vitro laboratory studies have not duplicated the problem presented by peritonitis due to the complex situation wherein susceptible Gram-positive cocci and penicillinase-producing Gram-negative bacilli exist in symbiosis.

In animals with peritonitis the beneficial effects of penicillin have been shown.[3,4] The clinical and laboratory observations have failed to establish an optimal dose. Because of the need for conservation of penicillin at the time of its introduction, most clinical studies of its use in various infections were aimed at establishing the minimum effective dose. In this regard, the revisions necessary, and the ultimate results in subacute bacterial endocarditis should be recalled. There is need for determination of the necessary dosage of penicillin for production of maximum effects in acute peritonitis.

Discovery of streptomycin revealed an antibiotic with many features surpassing penicillin for therapy of acute peritonitis, particularly because of its activity against Gram-negative bacilli. It is worth emphasizing that streptomycin possesses a wide anti-bacterial spectrum, including many strains of Gram-positive cocci, some of which are not sensitive to penicillin. Its higher toxicity and the quite rapid development of resistance in susceptible strains constitute its main deficiencies. Its definite value in experimental appendiceal peritonitis is well established.[3,9] The effects of streptomycin and penicillin are cumulative upon organisms susceptible to each.[10] In the treatment of acute infections the optimum therapeutic dose of streptomycin seems fairly well established at 0.5 gm. every four hours. This dosage in conjunction with large doses of penicillin, such as 100,000 units of mixed penicillin every two or three hours, would seem to be the most desirable antibiotic therapy available at present. A recent report on polymyxin indicates the existence of a new antibiotic substance with very active streptomycin-like activity against Gram-negative bacilli, and without the rapid development of resistant or "drug fast" strains.[12]

USE OF PENICILLIN ALONE

Clinical investigation of the value of penicillin as the only antibiotic factor in a group of patients representing all ages, and suffering from appendiceal peritonitis, has seemed desirable. Partly, this was due to the numerous objections to the sulfa drugs, and partly to the need for such a study in order to create a yardstick for comparison in any subsequent study of the clinical results with streptomycin. To this end a routine was established for the management of perforated appendicitis in one of the surgical divisions at the Los Angeles County General Hospital. The major features consisted of routine removal of the appendix through a McBurney incision, closure of the peritoneum without drainage, and the intramuscular administration of 100,000 units of penicillin every three hours, or with the same dose, but half given intramuscularly and half subcutaneously.[11] The ancillary management was carried out as described in the previous paragraphs. In one period there were 48 cases of acute perforated appendicitis and peritonitis with two deaths, neither of which was directly attributable to peritonitis. The same management, except that surgical operation was withheld, was used in 13 cases of appendiceal abscess, with no deaths and no operations for drainage. The majority of the operations done were carried out by the resident staff. There were no instances of subphrenic abscess, fecal fistula, or mechanical intestinal obstruction. This mortality of 3.3 per cent would seem to justify the belief that peritonitis can be quite successfully controlled by the application of an adequate program based on present knowledge.

SUMMARY

Acute bacterial peritonitis of enteric origin presents a clinical problem with numerous important disturbances secondary to the peritoneal sepsis. Proper management entails an appreciation of each of these, and an approximation of their correction whenever possible. A somewhat standard plan of treatment has been presented.

1930 Wilshire Boulevard.

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The Role of Tissue Permeability With Particular Reference To the Blood-Brain Barrier in Diseases of the Central Nervous System

ROBERT B. AIRD, M.D., *San Francisco*

THE attention of certain of my associates and myself has been directed both experimentally and clinically for several years to the possibility that permeability plays a role in disease processes of the central nervous system. We have been particularly interested in the blood-brain barrier and have developed methods for studying the permeability of this neurophysiological mechanism.

We have been able to show that the locus of this barrier resides, as Spatz[13] postulated, in the endothelial cells lining the walls of the cerebrovascular tree. Using the supravital dyes, Brilliant Vital Red and Trypan Red,[2] which uniquely stain these cells and which do not pass beyond the blood vessels to gain entrance into the nerve tissue proper, we have been able to lower the permeability of the blood-brain barrier and to prevent abnormal increases in the permeability of this barrier such as occur in many diseases of the central nervous system and which we have been able to produce in certain instances under controlled conditions in the experimental laboratory.

The neurophysiologic role of the blood-brain barrier is presumably fundamental in maintaining the homeostasis and conditions for normal metabolism within the central nervous system. The barrier also plays an important role in protecting the brain in various toxic conditions. For example, the barrier normally is impermeable to such electro-negative bacterial toxins as tetanus, diphtheria, botulinus and staphylococcus and such chemical agents as thiocyanates, neoarsphenamine, iodides and bromides.[10]

Studies on the blood-brain barrier indicate that practically all disease processes of the central nervous system tend to break the barrier down, that is, abnormally increase the permeability of the barrier. The results of the numerous studies[11] along this line may be listed in the following categories:

1. *Inflammatory Processes*
 - Meningitis
 - Encephalitis
 - Virus Infections
 - Abscess
 - Injury
2. *Toxic Processes*
 - Eclampsia
 - Acute Alcoholism
 - Theophyllin
 - Urotropin
 - Potassium Bromide
 - Urea
 - Bile Salts
 - Sodium Salicylate
3. *Physiologic Conditions*
 - High and low pH
 - High and low osmotic pressure
 - Menstruation
4. *Other Diseases of the Central Nervous System*
 - Tumors
 - Gliosis
5. *Tests and Surgical Procedures*
 - Craniotomy
 - Pneumoencephalogram
 - Lumbar puncture with forced drainage of cerebrospinal fluid

From the Divisions of Neurology and of Neurosurgery, the Electroencephalographic Laboratory of the University of California Medical School and the Spectrographic Laboratory of the University of California Medical School. These studies were made possible by grants from the Christine Breon Fund.

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Although the techniques and methods used in the majority of these studies may be criticized, the results in many studies and especially in those which have employed dyes, indicate that almost any disturbance within the central nervous system is associated with an increase in the permeability of the blood-brain barrier.

Our own studies have been directed along the following lines: to study the role of permeability in

1. Toxic diseases of the central nervous system.
2. Degenerative diseases of the central nervous system of possible toxic origin.
3. Cerebral concussion and other post-traumatic conditions.
4. Convulsive states.
5. Electroshock therapy.
6. Cerebro-vascular disorders.

Both experimental and clinical studies have been performed along these various lines. The traumatic and electroshock studies, for example, have been largely experimental, while the degenerative studies have been largely clinical. In all instances, however, the fundamental experimental observation that the permeability of the blood-brain barrier could be lowered by the supravital dyes, Brilliant Vital Red[1] and Trypan Red[2] has been used as a mechanism to alter the permeability in each condition studied and to test the relationship between permeability and other findings characteristic of the condition. For example, in using triphenyl phosphite as a convulsive agent in experimental epilepsy[3] we found that this compound was hydrolyzed readily in vivo and that two effects resulted from its breakdown products. The phenol fraction produced early convulsive effects at the cord level and the phosphorous acid fraction was selectively and preferentially absorbed by the gray matter of the central nervous system and caused late degenerative changes in the nervous system similar to such other esters of phosphorous acid as triorthocresyl phosphite, which produces a combined system degeneration of the spinal cord, and triorthocresyl phosphate, the contaminant responsible for the degenerative changes in cases of Jamaica ginger paralysis. If the animals were previously stained with Brilliant Vital Red, these toxic effects could be prevented. This illustrates our use of the dyes in toxic conditions of the central nervous system.

Our interest in the degenerative diseases of the central nervous system was stimulated by the concept that certain of these unexplained conditions might have a toxic origin. For example, this theory has been postulated for amyotrophic lateral sclerosis. Since the supravital dyes can be used with safety in man, we felt justified in trying them in these otherwise hopeless conditions with which we are so frequently confronted in neurologic practice. Such studies have been done without promises and only after a frank discussion of the situation with the patient and his family which would assure us of their cooperation in the prolonged follow-up that is essential in these conditions. Aside from testing the value of the dye therapy in these cases, we hoped that we might begin to sort out the large group of degenerative diseases and segregate those of toxic origin from the rest of the group.

Reference will be made only to one member of this group—amyotrophic lateral sclerosis.[4] Our results have been classified on a four-point scale:

1. No objective effect but possible subjective improvement.
2. Diminution of fasciculation.
3. Suggestive slowing of disease.
4. Process arrested and possible improvement in strength and weight.

On this basis, fasciculations were diminished in the majority, progression of the disease process was suggestively slowed in nearly 50 per cent and about one patient in six obtained an apparent arrest or even some improvement.

Although no final conclusions may be drawn from such data, the relationship between treatment and improvement in several patients appeared more than coincidental, especially in those patients in whom a recurrence of the disease process, following a discontinuance of the treatment, was again modified when adequate dye therapy was resumed. We have felt that the results were sufficiently encouraging to warrant further trial. Tentatively the same may be said for progressive muscular atrophy and progressive muscular dystrophy. Because of the variable and remissive course, characteristic of multiple sclerosis, it is impossible to arrive at any early conclusions in this condition. Our experience in other, more rare diseases of the central nervous system is too limited to permit any conclusions. Final conclusions as to the value of the dye therapy in these conditions and as to the significance of the results in establishing a toxic origin of them must await further trial and experience.

Our interest in cerebral concussion was stimulated by the concept that the maximal effect of a transmitted concussive blow might be expected at those points at which abrupt changes occur in the structure and density of the brain.[5,6] Shearing forces are known to produce their greatest effect at such junction points. Considering the anatomy of the brain, one would not expect major changes between cellular and extracellular elements, that is, along the cell membranes of the relatively homogeneous masses of the cerebral cortex. Where the cellular masses of the brain join other structures of different histological character, which are relatively large and fixed, such as the ependymal lining of the ventricular spaces and especially where the cellular masses of the brain make contact with their supporting vascular tree, one might expect greater shearing forces and neurophysiological changes. Disrupting effects at this latter point might be reflected in changes of vascular permeability, perivascular edema and nutritional alterations in the neighborhood effecting cerebral metabolism. Depending upon its severity and duration, neurophysiologic changes and even irreversible, degenerative changes might be produced. The perivas-

cular pathological changes described by Scheinker and Evans,[12,9] in more severe traumatic lesions of the brain would be in keeping with this hypothesis.

With this concept in mind, we have studied the effect of concussion on the vascular structure of the brain and have done so in experiments aimed to give us information on the permeability of the blood-brain barrier. The studies involved determinations of the distribution of cocaine by spectrophotometric methods in the brain and blood following the intravenous administration of this drug in control and traumatic groups of cats. As intimated, the object of these experiments was to determine whether or not alterations in the concentration of cocaine occurred in the central nervous system following cerebral concussion, which might reflect permeability effects of possible neurophysiologic and etiologic importance in the post-concussional state and post-traumatic head conditions.

Significant rises in the concentration of cocaine were found in the cerebral cortex after concussion without appreciable alterations in the blood concentration levels. These results indicate that cerebral concussion increases the permeability of the blood-brain barrier. Similar studies following preliminary injections of Trypan Red showed concentrations of cocaine in the post-concussional cortex which were equal to or lower than the corresponding control values, while again the blood concentration levels remained the same. It was concluded that Trypan Red effectively counteracted the permeability effect of cerebral concussion on the blood-brain barrier. It is also of interest in these studies that while approximately 80 per cent of the cats showed a cerebral dysrhythmia by electroencephalography three days after cerebral concussion, following preliminary Trypan Red injections the dysrhythmia either did not appear or appeared only in minor degree three days after traumatization. Since Trypan Red appears to counteract both the increase in permeability of the blood-brain barrier and the cerebral dysrhythmia associated with cerebral concussion, this dye may prove of practical value in determining the possible relationship between these neurophysiologic phenomena and the clinical symptoms characteristic of the post-concussional state. Inasmuch as Trypan Red may be used with safety in man, such therapeutic possibilities appeared worthy of exploration. Preliminary clinical studies, which are at present under way, suggest that this agent may have some beneficial effect on the post-concussive state.

Our interest in the use of the supravital dyes in the convulsive states was initiated by the discovery of Cobb and his co-workers[8] that Brilliant Vital Red would protect in both toxic epilepsy under controlled experimental conditions and also in human convulsive states. We have confirmed the observations of Cobb in both experimental and human epilepsy[1] and have continued to use this method of treatment as an adjunct to other anti-convulsive therapy when more routine methods have not proven adequate to control the convulsive state. Although not as potent as some of the modern anti-convulsive drugs now available, it is a valuable agent in those patients not fully protected by the usual methods, since it can be used in conjunction with them. We have also found that Trypan Red[2] is, in general, as effective as Brilliant Vital Red and because of its lower solubility and the fact that it is excreted more slowly than Brilliant Vital Red, it has proven of more practical value in actual practice.

The implications of the effectiveness of the supravital dyes in epilepsy are interesting and important. Why should an agent which alters the permeability of the blood-brain barrier and which does not itself gain entrance to the nerve tissue proper, have any effect on the convulsive state? The answer must be sought in the effect of the blood-brain barrier upon the physiological and biochemical state of the brain and consequently its effect in modifying the reactivity of the brain. When one considers the basic mechanisms known to modify the convulsive state, such as the acid-base balance and water balance of the central nervous system, it becomes apparent that many mechanisms which lower the permeability of tissue also afford protection in the convulsive states and, vice versa, that factors which increase permeability also increase convulsive susceptibility. Although the alteration of permeability in itself is presumably of the greatest importance in epilepsy induced by drugs, it is conceivable that some other changes associated with this alteration may be the precipitating factor in human epilepsy. Numerous complex physiologic and biochemical changes are associated with an alteration of the semipermeable characteristics of tissue membranes, and since these changes occur together, it is not possible to say that any single factor or combinations of factors is responsible for any resulting physiological effect. It seems likely that the convulsive state is a result of the whole complex of changes, that is, the changes associated with increased permeability in cortical tissue cause a more unstable and irritable state which, in turn, is characterized by an increased susceptibility to convulsions. As has been pointed out, those mechanisms, which are known to increase the permeability of tissue, such as alkalosis, hydration, anoxemia and inflammatory changes, are also known to lower the convulsive threshold. As a single mechanism of fundamental neurophysiologic importance in determining cellular nutrition and reactivity, permeability, or rather the complex of changes associated with alterations of permeability, offers an attractive hypothesis for the numerous, and otherwise unrelated, factors known to be of importance in modifying convulsive reactivity.

More recent investigations, possibly related to our earlier studies on the convulsive states, have been conducted in an attempt to elucidate the neurophysiologic basis of electroshock therapy.[7] Experimental studies with electroshock have been disappointing in that they have failed to explain the basis for the beneficial effects of this form of therapy in psychiatric conditions. Considering the anatomy of the vascular

tree of the brain and what is known concerning the transmission of electrical currents through tissues, one might postulate that a high percentage of the current traversing the brain would concentrate on and be transmitted along the vascular tree of the brain or in its blood stream. According to this concept, only as the current concentrated on the vascular tree in the cortex or escaped into the deep subcortical portions of the brain from the deeper blood vessels would the brain be stimulated. Since the effect on the vascular tree might be reflected in changes of the semipermeable characteristics of the membranes composing the blood vessel walls, as indeed has been suggested by neuropathological studies, we have initiated studies using techniques previously reported for measuring alterations in the permeability of the blood-brain barrier. The permeability of the blood-brain barrier was therefore studied in the same manner as mentioned previously, both before and after a series of electroshock treatments in cats. It was found, as suspected, that electroshock therapy did appreciably increase the permeability of the blood-brain barrier and that this effect persisted for days in contradistinction to the fleeting change of permeability which occurs in nerve tissue after its electrical stimulation. In another series of experiments, in which the cats were injected with Trypan Red before the series of electroshock treatments were given, it was found that the dye prevented the permeability changes of the first series of experiments. In these same experiments, a generalized cerebral dysrhythmia was obtained by electroencephalography in the initial shock experiments but was either not obtained or only slightly so in the second series of experiments after Trypan Red was used.

Since Trypan Red appears to counteract both the increase in permeability of the blood-brain barrier and the cerebral dysrhythmia associated with electroshock therapy, one wonders if it might not also counteract the beneficial effect of such therapy in psychiatric conditions. Although the practical difficulties of clinical investigation along these lines are obvious, suitable methods are being sought to test further the possible relationship between these persistent neurophysiologic phenomena and the beneficial effects of electroshock therapy.

An increase in permeability presumably occurs with the abnormal vasodilatation such as is associated with headaches of vascular origin, such as migraine and histamine headaches. This factor may account for the pipe-stem arteries, prolongation of symptoms and ineffectiveness of ergotamine tartrate when given late in an attack of migraine, for example. Again, this same permeability mechanism is presumably involved in conditions associated with perivascular disease, such as encephalitis lethargica, anterior poliomyelitis, the demyelinating diseases and the more severe post-traumatic head conditions already mentioned. Since such perivascular disease probably plays at least a secondary role in the pathological physiology of these conditions, supravital dye therapy, if it diminished or controlled this effect, might prove of some therapeutic value in them. Certain possibilities along these lines are now being investigated and it is hoped will be the subject of more specific reports at a later date.

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The Management of Acute and Chronic Pulmonary Abscess

Paul C. Samson, M.D.* and David J. Dugan, M.D., *Oakland*

Pulmonary abscess is a serious and unpredictable disease. While it has been estimated that from 25 to 35 per cent of patients become well spontaneously, the mortality has been from 30 to 50 per cent in most series of prior years.[1] We have long been opposed to the tendency of many physicians to separate the treatment of lung abscess into a medical phase and a surgical phase. In the not-too-far-distant past it was the custom to set a time limit, usually from six weeks to three months, for the period of purely "medical treatment." If the abscess was not cured by then, the case automatically became surgical. The effects of treating such a serious disease by this routine have been amply reflected in the appalling mortality statistics just quoted. There is now greater appreciation of the fact that pulmonary abscess is a suppurative disease and that because of this, surgical intervention becomes an ever-present possibility. The best results are obtained by the physician and thoracic surgeon working as a close team from the onset of illness. Observation is not treatment. Definitive therapy should be started at once. Radical change in treatment should be accepted by both physician and patient as an inherent part of the therapeutic regimen in this disease.

DIAGNOSIS

It should not be difficult to make a diagnosis of pulmonary abscess. While in a few cases the abscess is undoubtedly due to septic emboli, in the great majority it comes from aspiration, with blockage of a bronchopulmonary segment and distal suppuration. Pulmonary abscesses often follow operations around the mouth, nose, or face. In a majority of the few cases in which there was no such operation prior to the development of abscess, poor oral hygiene is evident.

Many patients show prodromal symptoms of generalized malaise, fever, and fairly localized thoracic pain. This will be followed within a few hours or a few days by sudden or increasing expectoration of large amounts of purulent sputum which layers out on standing. The sputum is not necessarily foul, but is frequently so at the onset. Roentgen studies in the frontal and lateral views will almost always clinch the diagnosis. It must be remembered that a fluid level or cavitation may not be seen on the roentgenogram. This usually means that the abscess has not yet emptied itself sufficiently.

ACUTE ABSCESS

The management of acute pulmonary abscess encompasses general hygienic care, the use of antibiotics and chemotherapy, and the promotion and maintenance of adequate drainage. Careful attention to the therapeutic details described in the following text has resulted in cure in approximately three out of four cases, without resort to surgery. In the other 25 per cent, surgical drainage has been necessary.

The intake of fluids, calories, vitamins and proteins should be adequate. Any deficiencies in oral intake should be made up by the parenteral route. The patients often develop considerable anemia. Iron mixtures may suffice, but if the hemoglobin falls to 70 per cent or below, whole blood transfusions are indicated.

The sulfa drugs and penicillin have been widely used in the treatment of pulmonary abscess. Probably their biggest contribution is in the prevention of invasive infection. The ancillary nature of this therapy must be emphasized. There has been no marked increase in the non-surgical incidence of cure since the beginning of widespread use of sulfa compounds and penicillin. There is some evidence to show that a combination of both drugs may be more efficacious than either one used alone.[5] Penicillin is administered by the aerosol and intramuscular routes. Drug therapy can be overdone, however, and is completely ineffective if the abscess does not drain properly. An abscess cavity may be temporarily sterilized, but it will not heal if a necrotic slough remains.

The most important single factor in cure is to establish adequate drainage. This is characteristic of an abscess in any portion of the body. Because all pulmonary abscesses possess a bronchial connection, it is possible that so-called internal drainage may suffice.

Adequate internal drainage is best initiated and maintained by modified postural drainage and by bronchoscopic aspiration. The type of postural drainage to be used must be individualized. In general, the patient should be instructed to assume the position which makes him cough most, four or five times during the day. Cough is a natural defense mechanism in raising secretions and is a good index as to whether or not postural drainage is being done in the most efficient position. The usual position of postural drainage with the patient hanging over the bed almost straight down from the hips may be harmful if the abscess is in the middle or upper lobes. The bronchoscope is an invaluable means of improving internal drainage. In the past bronchoscopy has been used far too infrequently during the acute phase of the abscess. Bronchoscopy should be one of the earliest therapeutic procedures employed. It has been stated that many patients are too sick to be subjected to bronchoscopy. Rather it should

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* Assistant Clinical Professor of Surgery, Stanford University School of Medicine, San Francisco, California.

be said that they are too ill not to be bronchoscoped. There are many who still are unconvinced as to the value of bronchoscopy. Such physicians either have not noted the benefit of an efficiently performed bronchoscopy, or they have been swayed by the operator's enthusiasm and allowed repeated bronchoscopies to be performed without appreciable improvement in the patient's condition. This cannot be held against the method, but is an indictment of the bronchoscopist's judgment. The bronchoscope is not an infallible instrument. One must not try to do the impossible with repeated aspirations if progressive clinical and roentgenologically demonstrable improvement does not ensue.

In brief, the bronchoscopist can be depended upon to do the following tasks: (1) Make an occasional diagnosis of unsuspected foreign body or neoplasm as the causative agent of the abscess; (2) remove obstructing secretions from the main and secondary bronchi; (3) elicit selective cough with further evacuation of secretions from the infected lobe; (4) shrink the congested edematous mucosa which in itself can cause visible obstruction of the bronchial airway; (5) pass long curved aspirators into the smaller bronchi of the diseased pulmonary segment and, rarely, directly into the abscess cavity.

In favorable cases the effects of bronchoscopy can be seen within a few days after the first aspiration. In many cases a second or third bronchoscopy at from five to seven-day intervals may be indicated. If, within 14 days after these procedures have been performed, there is still question as to the trend of the illness, it is unlikely that improvement has occurred and the type of treatment should be changed.

Once the patient with pulmonary abscess has come under the physician's care, improvement must be prompt and progressive or surgical operation should be undertaken. The improvement must be both clinical and roentgenologically observable. No abscess is doing well which remains unchanged on the roentgenograms for two or three weeks at a time, even though there has been amelioration of symptoms. Undoubted clinical improvement is manifested by decrease in the cough, reduction in the amount of sputum, a change in the character and odor of the sputum, a reduction in the fever, and an increased sense of well-being on the part of the patient. Should the fever continue at its previous level or should the secretions remain purulent and foul it is certain that drainage is ineffective. Improvement from the roentgen standpoint is manifested by loss of fluid levels, a decrease in the amount of surrounding pneumonitis, and progressive decrease in the size of the abscess cavity. The cavity which remains stationary or increases in size, particularly if there are associated symptoms of impaired drainage, is sufficient indication for surgical intervention.

The decision to initiate surgical intervention usually can and should be made well within six weeks of the onset of the disease. Brisk hemorrhage is an indication for prompt surgical drainage at any time it occurs.

Two pitfalls should be guarded against before operative drainage of a cavity is decided upon. Occasionally an abscess may develop which is merely an acute infective episode associated with chronic bronchiectasis. In such cases the patient does poorly following surgical drainage. A carefully taken history will help to avoid this mistake. Likewise a suppurating pulmonary cyst should not be drained unless the severity of the infection forces this action. Because of their mucosal lining, these cysts will not heal.

Most abscesses can be drained by a one-stage procedure. Since nearly all abscesses are on a pleural surface, adhesions rapidly form between the thoracic wall and the lung. These frequently cover a small area and accurate roentgen localization by means of fluoroscopy, frontal stereoscopic and lateral films is necessary prior to operation. The anesthetic may be either a combination of regional and local block with procaine or nitrous oxide and oxygen. A slightly curved incision is made and sections of one or two ribs together with the intervening intercostal bundle are removed. If the pleural space is not obliterated, an irritating pack of half-strength tincture of iodine or 1-1000 acriflavine solution should be placed against the parietal pleura as the first stage and left in place for approximately seven days. It is wise to recheck with roentgenograms after the first operation to be sure that the abscess is being approached properly. The abscess should be opened with a cautery and the contents evacuated simultaneously with suction. Bleeding is controlled by cautery or by suture-ligature. The cavity is packed lightly with gauze and repacked as necessary until healing takes place. In most instances where destruction of lung has not been too great the abscess cavity will gradually become obliterated by resolution and by re-expansion of the remaining lung. If the healing process is delayed much beyond six weeks and the cavity is clean, some type of filling with free fat grafts or with a pedicled muscle flap is advisable.

In rare instances severe hemorrhage may dictate a one-stage procedure, even in the absence of pleural adhesions. In such cases the area to be cauterized is encircled by mattress sutures which hold the lung in apposition to the chest wall.

Sudden thoracic pain, dyspnea, increased fever, and profound toxemia herald the sudden rupture of a pulmonary abscess into the pleural cavity. In our opinion this serious complication constitutes a surgical emergency. Any temporizing with repeated aspirations and the injection of sulfa drugs or antibiotics is almost certain to end disastrously. Likewise, closed intercostal drainage in this type of acute empyema is unsatisfactory in the extreme. Such treatments frequently result in spreading anaerobic cellulitis or fascitis of the thoracic wall and the mortality then is very high. The treatment of choice is to ignore the abscess for the time being and to open the pleural cavity widely by a long posterior resection of the 8th or 9th rib.[3] Rapid evacuation of infected contents is accomplished and multiple Pen-

rose drains are introduced into the pleural cavity, supported by a large pack. If, and when, the lung re-expands the abscess can be dealt with as necessary at a later date.

CHRONIC PULMONARY ABSCESS

It may be difficult to distinguish accurately between acute and chronic abscess. Pathologically speaking, chronicity in infection means the formation of mature scar tissue and the predominance of round cell infiltration over polymorphonuclear invasion. In pulmonary abscess chronicity is characterized by increased pulmonary destruction and fibrosis of the parenchyma with extensive pneumonitis and bronchiectasis. Some of these changes may occur as early as six weeks after the onset if treatment has failed of undoubted improvement or of cure.

Attention to general hygienic measures is more important in chronic than in acute pulmonary abscess. In particular, severe anemia and protein deficiency inevitably will develop unless proper preventive measures are taken.

In the treatment of chronic abscess bronchoscopy always should be performed for diagnostic purposes and to improve drainage. In rare instances one, or several, bronchoscopies may effect a cure.[4] If the cavity does not have thick walls and if the surrounding parenchyma seems normal, external drainage may be considered. If, however, the area of infection casts a dense shadow with multiple small areas of excavation, if the surrounding parenchyma seems contracted, or if the abscess is thick-walled or unduly large, external drainage probably will fail. As a general rule, the more chronic the abscess the less the chance of cure by drainage procedures. In any event bronchograms should be made before external drainage is decided upon. In the presence of associated bronchiectasis or of bronchial obstruction, external drainage will not succeed.

Signs of chronicity may develop in an abscess which has been inadequately drained. Fistulae will remain widely patent and develop indurated orifices; heavy purulent discharge will persist. While we cannot prove it statistically we have the impression that a true septic infarct which cavitates is less likely to heal following surgical drainage than is an abscess which results from aspiration. In the former instance it may be that the surrounding parenchyma has a permanently poor blood supply which is a factor in the development of chronicity. Occasionally one may be tempted to perform secondary drainage procedures on an abscess which is not "clearing up" properly. Those procedures are frequently unsuccessful because of the underlying irreversible pulmonary damage. In fact, Churchill has failed to cure any recurrent abscess by re-establishing drainage.[2,6] Further drainage may be indicated if a secondary acute abscess develops as an extension of the original process.

It has become increasingly evident that many cases of chronic pulmonary abscess should be treated primarily by pulmonary resection rather than by external drainage. Lobectomy, performed in the modern manner, carries far less hazard than the external drainage of a chronic abscess. If preoperative survey shows an entire lobe to be damaged, total lobectomy should be performed. If the disease is definitely localized, segmental lobectomy may be indicated. The lingular division of the left upper lobe and the superior (dorsal, apical) divisions of the lower lobes lend themselves particularly well to segmental resection. If all lobes on one side are involved, total pneumonectomy by individual ligation is infinitely preferable to attempted cautery penumonectomy. Even though external drainage has been attempted and has failed, resection still can be accomplished. The hazard, however, is increased somewhat because of the greater chance for intrapleural and wound infection. In performing an operation of this type, separate instruments should be used to free up the draining sinus, excise the epithelial portion, invert the remainder and close the overlying skin. The chest is then opened through a separate incision, the operator using clean gowns, gloves, and instruments.

SUMMARY

The hazards of pulmonary abscess are discussed and the necessity for early definitive therapy is stressed.

The treatment of acute abscess is outlined, including provisions for general hygienic care, the role of chemotherapy and the supreme importance of adequate drainage.

The role of bronchoscopy is emphasized in establishing and maintaining curative "internal drainage."

With proper attention to the above details approximately 75 per cent of patients with acute pulmonary abscess can be cured without resort to surgical operation.

The indications for external surgical drainage of acute abscess are listed.

The irreversible pulmonary changes associated with chronic pulmonary abscess are described.

The surgical problem in chronic abscess is contrasted with that in acute abscess.

The value of pulmonary resection in the treatment of chronic pulmonary abscess is stressed.

2938 McClure Street.

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Analysis of Fatal Cases of Poliomyelitis

WALTON M. EDWARDS, Major, M.C., U. S. Army*

POLIOMYELITIS has been a problem among military personnel since the expansion of the Army. During the period 1940-1946, there was a total of 1,654 cases with 286 deaths. (Table 1.)

Poliomyelitis in its etiological, diagnostic and therapeutic aspects has been covered in the literature[7,12,13] and this paper is concerned with the statistical analysis of data available in 149 fatal cases from the United States Army hospitals† during 1944-1945. Reports of additional cases are available but are not included because of incomplete clinical records.

INCIDENCE

The incidence and mortality among military personnel compared with reports from the United States Public Health Service for the general population is shown in Table 1. The incidence in the Army is lower, as would be expected, since different age groups are involved. The mortality among military personnel is higher, the average for the Army for the period 1940-1945 being 17 per cent, while that for the general population was 9 per cent. This would indicate that the disease has a high mortality among adults of military age.

TABLE 1.—*Incidence of Poliomyelitis in U. S. Army Compared with the United States*

Year	Number Cases U.S. Army	Number Cases United States	Deaths U.S. Army	Deaths United States	Per Cent Mortality U.S. Army	Per Cent Mortality United States
1940	8 (1:42,000) *	9,826‡ (1:14,000)	2	1,026	25%	10%
1941	45 (1:30,000)	9,086 (1:14,000)	7	807	16%	9%
1942	62 (1:52,000)	4,033 (1:32,000)	5	561	8%	14%
1943	248 (1:28,000)	12,449 (1:12,000)	49	1,151	20%	9%
1944	350 (1:22,000)	19,029 (1:6,800)	59	1,361	17%	7%
1945	680 (1:11,000)	13,619 (1:10,000)	129	1,186	19%	9%
1946	261 (1:8,000)	25,191 (1:5,400)	35		13%	
					17%	9%

* The figures (1:42,000) denote one case of poliomyelitis to 42,000 persons. Figures are based on the approximate strength of the Army and the population of the United States. Data pertaining to Army personnel are preliminary and are obtained from two separate and not completely comparable sources. The cases shown for 1943-1946 and the deaths for 1944-1946 are derived from the periodic summary report, weekly statistical health report, and presumably include all cases of and deaths due to poliomyelitis, regardless of whether poliomyelitis was the cause of admission. These data may also erroneously include some cases on the basis of admitting diagnoses of poliomyelitis which were subsequently changed. Cases for 1940-1942 are based on tabulations of individual medical records where poliomyelitis was the cause of admission, while deaths for 1940-1943 are based on tabulations of individual medical records by cause of death. Use of these several sources makes the figures shown for per cent of mortality rather uncertain.

‡ From United States Public Health Service.

* Chief of communicable disease section, Letterman General Hospital, San Francisco, California.

† One female military dependent is included.

1. *Geographical Distribution:* The geographical occurrence of the cases is shown in Table 2.

2. *Age:* The recorded ages in 129 patients ranged from 17 years to 36 years, as shown in Table 3.

3. *Color:* Race is recorded in 147 patients. There were 139 whites and 8 negroes.

4. *Constitutional Factors:* The actual weights are not recorded in each case. However, the state of nutrition of military personnel may be assumed to be good. This is in accordance with findings of early writers on poliomyelitis, who state that the healthy, well-developed individual appears to be most susceptible to the disease.

TYPES OF CASES

In grouping of cases, the following classifications were used:

1. *Bulbar Spinal Type:* This group comprises patients with definite paralysis or paresis of muscles supplied by the spinal or cranial nerves.

2. *Bulbar Type:* This group includes patients with paralysis or weakness of the muscles supplied by the cranial nerves only.

3. *Encephalitic Type:* In this group are included cases characterized by cerebral involvement, usually indicated by high fever, prolonged stupor, disorientation, coma or convulsions.

One hundred and twenty-two were of the bulbar spinal type, 24 of the bulbar type, and three of the encephalitic type. There were 14 patients included among the bulbar spinal cases, who died of respiratory failure. These patients developed paralysis of the extremities, which ascended to produce dyspnea

TABLE 2.—*Area of Admission of 149 Selected Cases Terminating in Death, 1944-1945*

Location	No. of Cases	Per Cent
United States	51	34%
Philippines	42	28%
China, Burma, India	28	19%
European Theater	16	11%
Italy, Sicily	9	6%
North Africa	2	1%
Persian Gulf	1	1%

TABLE 3.—*Age Group Distribution in 129 Fatal Cases of Poliomyelitis*

Age	No. of Patients	Per Cent of Total
17-19	11	8
20-24	62	50
25-29	43	33
30-34	11	8
Over 35	2	1

and cyanosis. No notation of specific cranial nerve involvement appears in the clinical records of these patients, but all became comatose and died in the respirator, and it is felt that the infection should be classified as of the bulbar spinal type.

SYMPTOMS‡

It is generally stated that the symptoms of poliomyelitis are variable, and this is borne out by an analysis of this series.

Duration of Symptoms: Table 4 shows the duration of symptoms prior to hospitalization. Ninety-five per cent of the patients were hospitalized within five days of the onset of their symptoms. The proximity of medical officers to troops was no doubt responsible for early hospitalization.

TABLE 4.—*Duration of Symptoms in Days Prior to Admission to First Medical Installation in Series of 149 Fatal Cases of Poliomyelitis*

Duration	No. of Cases	Per Cent	Duration	No. of Cases	Per Cent
1 day	42	31	6 days	1	
2 days	39	27	7 days	2	
3 days	37	26	8 days	1	5
4 days	6	5	9 days	1	
5 days	8	6	10 days	1	

General Symptoms: In 137 patients, 92 per cent, the temperature was elevated at the time of hospitalization. The range of temperature varied considerably. There were 29 patients with temperatures above 104° F., including one in whom the temperature reached 110° F. In 12 patients there was no note of fever in the clinical records. It is very probable that fever was present, but not recorded.

Other general constitutional symptoms of frequent occurrence were headache, stiff neck, and weakness of the extremities as shown in Table 5. Hyperalgesia of the back, shoulders, pelvis and extremities were fairly common early in the disease. Skin rashes were described in two patients. In one the rash was morbilliform, generalized and appeared early in the disease and lasted about one day. In the other, the rash was urticarial and of short duration.

TABLE 5.—*Relative Frequency of General Symptoms*

Symptom	No. Having Symptom	Per Cent of Total
Fever	137	92
Headache	112	76
Stiff Neck	112	76
Weakness of extremities	96	64
Hyperalgesia	93	63
Backache	76	52
Tremor	25	17
Hypesthesia	17	11
Drowsiness	9	6
Convulsions	6	4
Lymphadenopathy	4	3
Rash	2	1

‡ Symptoms will be listed under the various systems for the purpose of classification. However, it is the opinion of other writers[3] on poliomyelitis that such manifestations as headache, vomiting, weakness, hyperalgesia, are all indicative of central nervous system disturbances and not of extraneural disease.

Gastro-intestinal Symptoms: Symptoms referable to the gastro-intestinal tract are shown in Table 6. Vomiting was the most common. Abdominal distention was often severe and required decompression measures and prostigmine for relief. One patient, who was eight months pregnant, was thought to have intestinal obstruction because of the severe abdominal distention and vomiting, and surgical intervention was considered. Two patients were admitted with a diagnosis of acute appendicitis.

TABLE 6.—*Gastro-Intestinal Symptoms*

Symptom	No. of Patients	Per Cent of Total
Vomiting	78	53
Abdominal distention	44	29
Abdominal pain	26	18
Constipation	16	10
Diarrhea	7	5

Respiratory Symptoms: The occurrence of respiratory symptoms is shown in Table 7. Dyspnea and cyanosis were frequent and were attributable to bulbar paralysis, involvement of the muscles of respiration or pulmonary involvement. Cyanosis accompanying the dyspnea was usually a terminal feature.

TABLE 7.—*Respiratory Symptoms*

Symptom	No. of Patients	Per Cent of Total
Dyspnea	128	86
Cyanosis	105	70
Nasopharyngitis	34	23
Sore Throat	23	16
Cough	14	10
Bronchitis	10	6

Genito-urinary Symptoms: Symptoms referable to the genito-urinary system are shown in Table 8. Urinary retention occurred in 73 patients (51 per cent), and persisted until death in 57 patients (38 per cent). There was spontaneous recovery of bladder control in 13 patients (9 per cent). Incontinence of urine developed in three patients (2 per cent). It has been stated by other writers[9] that retention of urine is a transient phenomenon and usually disappears during the course of the disease. In this series, in which all the cases were fatal, many of the patients died early in the illness. Hence it is difficult to appraise the duration of this manifestation. Most of those who regained bladder control did so during the first week. The longest interval of time required for recovery of bladder control was 21 days. In three patients, frequency and dysuria were the initial presenting symptoms and they were admitted with a diagnosis of prostatitis.

TABLE 8.—*Genito-Urinary Symptoms in 149 Fatal Cases of Poliomyelitis*

	No. of Cases	Per Cent
Inability to urinate	73	49
Persistent urinary retention	57	38
Recovery of bladder control	13	9
Incontinence of urine	3	2
Dysuria and frequency	3	2

Neurological Symptoms: The occurrence of neurological symptoms is shown in Table 9. The various manifestations often resembled those seen in the other diseases to which the symptoms were erroneously ascribed in early diagnosis, as will be noted later in Table 19. Stiff neck was more frequent than stiff back, which is contrary to textbook teachings.[8] Kernig's sign was noted in 40 patients, although it is very probable that it occurred more frequently, but was not recorded in the clinical records.

TABLE 9.—*Neurological Manifestations*

Sign	No. of Patients	Per Cent of Total
Nuchal rigidity	93	63
Disorientation	50	34
Muscle fibrillation	40	27
Kernig's sign	40	27
Stiff back	26	18
Head drop	16	11
Sensory changes	5	3

Paralysis: Distribution of Paralysis: The paralysis of muscle groups is shown in Table 10. One hundred twenty-two patients developed paresis or paralysis of the extremities. Paralysis of the intercostal muscles occurred in 69 per cent of the patients, and was more common than paralysis of the diaphragm (42 per cent), or abdominal muscle paralysis (14 per cent). Cranial nerve involvement is shown in Table 11. The tenth cranial nerve (vagus) was most commonly affected. Difficulty in swallowing was observed in 93 patients (63 per cent), as shown in Table 12. It appeared early and persisted until death in 73 patients (49 per cent). In 17 patients (13 per cent), it developed terminally. It was transient in only three patients. Difficulty in swallowing has been stated by other writers[2] to be a transitory phenomenon. Since death occurred in all these cases here reviewed, it is difficult to appraise the duration of this manifestation.

Interval Between Onset and Paralysis: This time interval was established in 122 patients. This relationship is shown in Table 13. It occurred within four days after the onset of the illness in 87 per cent of the patients, and during the first day of the disease in 14 per cent. Sudden paralysis in a previously healthy individual was observed. Several patients experienced paralysis in attempting to get out of bed to go to the latrine. One patient suddenly noted paralysis of his legs in getting out of a vehicle after a convoy trip over the Burma Road. Prodromal symptoms such as upper respiratory infections, malaise, or fatigue were present in many patients. It appeared that as long as an elevation of temperature persisted there was a possibility of the paralysis extending to uninvolved muscles.

Reflexes: Ninety-three patients (63 per cent) exhibited abnormal deep reflexes at the time of hospitalization or shortly thereafter. In 64 patients (42 per cent), absence of superficial reflexes (abdominals and cremasterics) developed during the course of the disease. The superficial reflexes invariably disappeared as the paralysis ascended to produce bulbar symptoms. Abnormal deep or superficial reflexes were not recorded in any of the patients with the pure bulbar type or encephalitic type of disease.

TABLE 10.—*Distribution of Muscular Paralysis in 149 Fatal Cases of Poliomyelitis*

	No. of Cases	Per Cent
Arms and legs	88	59
Arms only	19	13
Bilateral	13	
Right	4	
Left	2	
Legs only	15	10
Bilateral	13	
Left	2	
Intercostal muscles	103	69
Diaphragm	63	42
Shoulder girdle	25	16
Abdominal muscles	22	14
Neck muscles	18	12

LABORATORY DATA

1. *Spinal Fluid:* The spinal fluid examinations were often incomplete, and data as to gross appearance, cell count, chemistry, serology, and colloidal gold were not available in all clinical records. The spinal fluid findings are shown in Tables 14 and 15.

TABLE 11.—*Cranial Nerve Paralysis in 149 Fatal Cases of Poliomyelitis*

		No. of Cases	Per Cent
II	Diminution of vision	5	3
III	Inequality of pupils	8	6
IV, VI	Ptosis of lids	7	5
VIII	Nystagmus	16	11
V	Weakness of jaw	3	2
IV, VI	Strabismus	8	5
	Diplopia	9	6
VII	Facial weakness	19	13
IX, X	Absent gag reflex	9	6
	Inability to clear throat	97	65
	Weakened voice	78	52
	Difficulty in swallowing	93	63
XI	Weakened neck muscles	18	12
XII	Tongue deviated	14	10

TABLE 12.—*Paralysis of Muscles of Deglutition in 149 Fatal Cases of Poliomyelitis*

Number of cases	93
Early onset and persisting until death	73
Developing with terminal phase	17
Transitory difficulty	3

TABLE 13.—*Interval Between Onset of Symptoms and Paralysis of Extremities*

	No. of Cases	Per Cent
1 day	17	14
2 days	45	37
3 days	32	26
4 days	12	10
Over 4 days	16	13
Total	122	
No paralysis of extremities	27	18

TABLE 14.—*Spinal Fluid Findings in 149 Fatal Cases of Poliomyelitis*

	No. of Cases	Per Cent
Gross appearance (124 cases)		
Clear	101	82
Opalescent	23	18
Cell Count (132 cases)		
Normal	18	14
10-50	24	18
50-100	16	12
100-500	59	45
500-1,000	10	8
Over 1,000	6	5
Lymphocytosis	55	56
Polymorphonucleosis	43	44
Protein (57 cases)		
Normal	9	15
40-80 mgm.	16	28
80-100 mgm.	14	25
Over 100 mgm.	18	32
Sugar (74 cases)		
Normal	41	55
70-100 mgm.	25	34
Over 100 mgm.	8	11
Chlorides (as NaCl) (21 cases)		
Normal	12	57
Elevated	8	38
Lowered	1	5
Colloidal gold curves (24 cases)		
Normal	9	39
Abnormal	15	61
Wassermann reaction (17 cases)		
Normal	16	94
Positive	1	6

TABLE 15.—*Spinal Fluid Findings in Bulbar Type Cases in 149 Fatal Cases of Poliomyelitis*

Spinal Fluid	No. of Cases	Per Cent
Cell Count (19 cases)		
Normal	6	32
10-50	3	15
50-100	3	15
100-500	6	32
500-1,000	1	4
Over 1,000	0	0
Cellular morphology (11 cases)		
Lymphocytosis	7	
Polymorphonucleosis	4	

Gross Appearance (124 patients): The spinal fluid was clear in 101 observations (82 per cent), and opalescent in 23 (18 per cent).

Cell Count (132 patients): Most laboratories accept the upper limits of normal as ten cells per cubic millimeter. The cell counts at the time of the initial spinal fluid examination, during the first week of the disease, were found to be elevated in 114 patients (86 per cent), and normal in 18 (14 per cent). Of the patients having normal cell counts, four showed an increase on subsequent examinations. The majority of the patients exhibited cell counts between 100 and 500 cells per cubic millimeter. The highest figure reported was 1,900 cells per cubic millimeter. Lymphocytes predominated in the majority of cases. It has been stated[7] that early in the disease the spinal fluid response is a preponderance of polymorphonuclear cells, and later there is a lymphocytic response. This was not observed in this series. Among the patients with the pure bulbar type of the disease, normal spinal fluid findings occurred in 32 per cent, and the cell counts when elevated were under 100 cells per cubic millimeter, with lymphocytes predominating in the majority of cases. No counts over 1,000 cells per cubic millimeter occurred in this latter group.

Quantitative Proteins (57 patients): Eighty-five per cent had spinal fluids with elevated protein content. Normal values were obtained in 15 per cent. There was no correlation between the protein content and the cell count.

Quantitative Sugar (74 patients): There were 33 patients (45 per cent), whose spinal fluid was found to have elevated sugar content, and of these, eight patients (11 per cent) had values above 100 mg. per cc. In no case was the spinal fluid sugar below normal. It has been reported that a highly elevated sugar content connotes a poor prognosis.[11] In this series, 87 per cent of the patients died within the first ten days of illness and the length of life could not be prognosticated from the spinal fluid sugar content.

Quantitative Chlorides: This was determined in only 21 patients. Normal values were found in 12 patients (57 per cent), and elevated values in eight patients (38 per cent). In only one instance was there reduction below the normal value.

Wassermann Reaction: The reaction to Wassermann test of the spinal fluid reported for 17 patients, was found to be negative in 16 and positive in one. There was no other evidence of syphilis in this one patient.

Colloidal Gold: Colloidal gold studies were reported in 24 patients, and the curves were abnormal, with no constant pattern, in 15 patients and normal in nine patients.

2. *Urine:* Urinalysis was performed in 98 instances and albuminuria ranging from 1+ to 4+ was encountered in 18 (21 per cent).

3. *Serology:* A Wassermann test of the blood was done in 17 cases and reactions in all were negative.

4. *Sedimentation Rate:* Blood sedimentation rates have been reported to be normal in poliomyelitis.[4] This determination was recorded in 23 cases shortly after hospitalization and was found to be normal in five (22 per cent), and elevated in 18 (78 per cent).

5. *Hematology:* Leukocyte counts were made in 124 cases at the time of hospitalization. Normal values (5,000 to 10,000) were noted in 41 (33 per cent). The majority of patients had leukocyte counts between 10,000 and 20,000. There were seven with counts above 20,000.

A summary of laboratory findings is shown in Table 16.

MORTALITY

The causes of death and the number of days by which death followed the onset of symptoms are shown in Tables 17 and 18. Autopsies were performed in 120 cases (80 per cent).

TABLE 16.—*Laboratory Findings in 149 Fatal Cases of Poliomyelitis*

	No. of Cases	Per Cent
Serology (17 cases)		
Normal	17	100
Sedimentation rate (23 cases)		
Normal	5	22
Elevated	18	78
Hematology (124 cases)		
Leukocyte count		
5,000-10,000	41	33
10,000-15,000	51	41
15,000-20,000	23	20
Over 20,000	7	6
Abnormal cells (Malaria)	2	
Urine (98 cases)		
Normal	80	79
Albuminuria	18	21

TABLE 17.—*Day of Death After Onset of Symptoms in 149 Fatal Cases of Poliomyelitis*

Day of Death (From Onset of Symptoms)					
1 day	3	10 days	4	22 days	1
2 days	4	11 days	3	23 days	1
3 days	24	12 days	2	41 days	1
4 days	18	13 days	2	56 days	1
5 days	20	14 days	1	58 days	1
6 days	14	15 days	1	85 days	1
7 days	18	16 days	1	130 days	1
8 days	18	17 days	1	135 days	1
9 days	5	19 days	1	170 days	1

TABLE 18.—*Principal Causes of Death in 149 Fatal Cases of Poliomyelitis*

Respiratory failure	99
Respiratory failure—Pneumonia	38
Pneumonia secondary cause of death	30
Pneumonia primary cause of death	8
Penicillin treated	27
No penicillin	11
Respiratory failure—Pulmonary edema	2
Respiratory failure—Pyelonephritis	1
Respiratory failure—Pneumonia, atelectasis	3
Respiratory failure—Pneumonia, myocarditis	2
Respiratory failure—Malaria	1
Severe toxemia	3

CLINICAL PICTURE

From the data presented, it is obvious that there is nothing pathognomonic of the disease. No single symptom or sign was present in all cases. Temperature elevations were recorded in 92 per cent of the cases.

Spinal fluid cell counts were normal in 14 per cent. Spinal fluid protein determinations were normal in 15 per cent, and sugar values were normal in 55 per cent.

Symptoms of importance were headache, stiff neck, weakness of the extremities, hyperalgesia and backache. Among the gastro-intestinal symptoms of frequent occurrence were vomiting, abdominal pain and distention. Respiratory, genito-urinary, and nervous symptoms have been listed.

The diagnosis of poliomyelitis is difficult, as is shown in Table 19, which lists the impressions prior to the final diagnosis.

TABLE 19.—*Diagnosis Considered at Time of Admission and Subsequent Impressions Prior to Final Diagnosis in 149 Fatal Cases of Poliomyelitis*

Alcoholism	1	Psychoneurosis:	
Appendicitis	2	Battle fatigue	1
Arthralgia	1	Anuria	1
Arthritis	1	Hysteria	7
Bell's Palsy	1	Jitters	1
Dengue	13	Pyrexia, cause undetermined	21
Diphtheria	4	Pyelonephritis	1
Encephalitis	10	Retropharyngeal abscess	1
Gastro-enteritis	8	Salmonellosis	1
Guillain-Barre	9	Sandfly fever	3
Hepatitis	5	Sciatica	1
Hookworm	1	Sinusitis	3
Infectious mononucleosis	1	Spinal cord tumor	1
Influenza	5	Subacute bacterial endocarditis	1
Laryngotracheo-bronchitis	4	Subarachnoid hemorrhage	1
Malaria	12	Tetanus	1
Meningitis	36	Thrombophlebitis	1
Myasthenia gravis	1	Tick bite fever	1
Nasopharyngitis	18	Toxemia of pregnancy	1
Pelvic abscess	1	Typhoid fever	1
Periodic family paralysis	1	Undulant fever	1
Pneumonia	4	Vaccination reaction	1
Prostatitis	2		

Thirty per cent of the cases were correctly diagnosed at the first medical installation at which the patient was observed. On physical examination, several findings were important. Stiff neck was frequent. Abnormal deep and superficial reflexes were present in the majority of cases. The disappearance of abdominal and cremasteric reflexes, which had been present earlier in the disease, were consistently associated with progressive bulbar involvement. Muscle paralysis appeared suddenly and was complete in some patients. In others, it was progressive over several days and in this group the fever was usually continuous. As long as fever continued, it was probable that the paralysis would spread. The accumulation of mucus in the throat, weakened voice and difficulty in swallowing directed attention to involvement of the tenth cranial nerve. The involvement of other cranial nerves has been listed.

In regard to the laboratory aids in the diagnosis, the spinal fluid examination, characterized by an increase in the cell count and protein content, provided important information. The average cell count was between 100 and 500 cells per cubic millimeter, but considerable variation occurred. In 85 per cent of the cases in which spinal fluid was tested for protein content the content was found to be elevated; in 32 per cent it was more than 100 mg. per cc. Hemograms revealed leukocyte counts between 10,000 and 20,000 in the majority of cases.

TREATMENT

Treatment instituted is included under the headings of (1) Special measures, (2) Symptomatic nonspecific measures and (3) Treatment based on errors in diagnosis. Since all cases were fatal, it is difficult to evaluate any method of therapy.

1. *Special Measures:*

Respirator: The respirator was used in 98 cases. The length of life in the machine and the sensorium at the time of its use is shown in Table 20. Eighty-one patients (82 per cent) died within the first three days. Three died while being transported to the respirator. It was used on 19 patients for whom no data as to the condition of the respiratory muscles appeared in the clinical record. The use of the respirator has been adequately covered.[14] It is common knowledge that the bulbar type is the most unfavorable form of the disease for the use of the respirator. The failure of the respirator, as evidenced by the high mortality within the first few days, is in accordance with the results of other observers.[4] There were some bulbar manifestations in all except the three cases of the encephalitic type of the disease. All patients surviving more than one week in the respirator were rational at the time they were put into it. The length of life of the patients who were rational at the time of use of the respirator, as compared with those who were irrational, is shown in Table 21. It would appear that the state of the sensorium at the time of use of the respirator was important.

Whole blood, plasma, albumin, antipoliomyelitis serum: These measures were used in 20 patients, the principle being to provide antibodies by using whole blood, plasma or anti-poliomyelitis serum, and to reduce edema of the nervous system by the use of albumin. The value of antibodies is questionable,[1] and no references are available regarding the use of albumin in poliomyelitis.

TABLE 20.—*Length of Life in Respirator in a Series of 149 Fatal Cases of Poliomyelitis*

	No. of Cases
Length of Life in Respirator	
Under one hour	7
1-12 hours	16
12-48 hours	48
3 days	10
4 days	1
5 days	2
6 days	2
8 days	1
9 days	1
13 days	1
16 days	2
40 days	1
56 days	2
73 days	1
125 days	1
135 days	1
170 days	1
Total	98
Died en route to respirator	3
Placed in respirator, but no note regarding respiratory muscles	19

TABLE 21.—*Sensorium at Time of Placing Patient in Respirator in a Series of 149 Fatal Cases of Poliomyelitis*

	No. of Cases
Rational	54
Irrational	44
Average length of life in respirator (Cases surviving under 8 days)	
Rational group	46 hours
Irrational group	19 hours

Kenny Principles: Twenty-three patients were treated by the application of heat to muscles exhibiting spasm. The evaluation of this method is difficult, since all cases were fatal. From notes in the clinical records, one gains the impression that the method was a failure. The literature contains numerous references to the Kenny principles,[6] and it will not be discussed in this paper.

Tracheotomy, intubation, bronchoscopic drainage, intratracheal suction: One patient was tracheotomized and another was intubated immediately following hospitalization because of respiratory distress, and death occurred within a few days after these operative procedures. In both patients the disease was erroneously diagnosed as acute laryngotracheobronchitis. Bronchoscopic aspiration was performed on two patients who developed atelectasis and pneumonia during protracted periods in the respirator and both died within 24 hours following the procedure. Intratracheal suction was performed on three patients, but all died within a few days of respiratory failure.

Spinal Drainage: Two patients were given hypertonic dextrose, and concomitant continuous spinal drainage was performed, without any degree of success.

Orthopedic Measures: The orthopedic aspects of the treatment will not be discussed in this paper.

2. *Non-Specific Therapeutic Measures:*

Oxygen: The administration of oxygen by mask, nasal catheter, or tent was used in 102 patients, the indications being severe toxemia, dyspnea, or cyanosis.

Penicillin: Penicillin was administered to 66 patients on an empirical or prophylactic basis with a view to combating secondary bacterial infection. Pneumonia was present on autopsy findings in 38 patients. Of these, 27 had been given penicillin. This would indicate that penicillin will not prevent pulmonary involvement in such cases. All patients exhibiting pneumonia at autopsy had been in the respirator. Bacterial studies to determine the type of the pneumonia were not available.

Sulfonamides: Sulfonamides by oral or intravenous routes were administered to 60 patients. The danger of sulfonamides in poliomyelitis has been stressed by Toomey.[10]

Other non-specific therapeutic measures included parenteral fluids, amigen, vitamins, stimulants, sedatives, analgesics, and drugs such as prostigmine, atropine, aminophylline, and streptomycin.

3. *Therapeutic Measures Based on Errors in Diagnosis:*

Penicillin Intrathecally: Penicillin intrathecally was administered to seven patients. The rationale

for this therapy was apparently based on a presumptive diagnosis of bacterial meningitis. One patient had a normal spinal fluid at the time of initial lumbar puncture, but was given 10,000 units of penicillin intrathecally. Within the next few hours the meningeal signs and symptoms increased and the temperature rose to 105° F. The following day the spinal fluid was found to be opalescent with 450 cells per cubic millimeter, all polymorphonuclears, and the patient died within 24 hours. Another patient died suddenly five hours after the administration of 10,000 units of penicillin intrathecally. The hazard of intrathecal penicillin has been reported by other observers.[5]

Other Erroneous Therapeutic Measures: One patient was given 300,000 units of tetanus anti-toxin by combined intrathecal and parenteral routes because of a diagnosis of possible tetanus. Another patient, with a diagnosis of hookworm infection because of the presence of hookworm ova in the stools, and paresthesias of the feet, was given tetrachlorethylene followed by saline purgations. His legs collapsed while he was making one of frequent trips to the latrine. Acute poliomyelitis finally was diagnosed and the patient died two days later. Another patient, who had been in combat on Luzon for 78 days, was examined in a collecting station because of weakness of the arms and legs. Upon a diagnosis of "battle fatigue" he was given a total dose of 2 gm. of sodium amytal intravenously. When the sedation effect disappeared, this patient's arms and legs were completely paralyzed. Respiratory difficulty required the use of the respirator and the patient died. One hundred thousand units of diphtheria anti-toxin was given to another patient who was thought to have laryngotracheobronchitis caused by diphtheria. There were seven cases in which a diagnosis of hysteria was based upon complaints of hyperalgesia and weakness of the arms and legs. These patients were treated on a sick-in-quarters status before paralysis developed and a final diagnosis of poliomyelitis was made. Another patient with generalized tremor of the arms and legs was returned to duty (after sedation) with a diagnosis of "jitters." Paralysis of both arms and legs developed and the patient died of respiratory paralysis three days later. Because of the incidence of dengue fever, malaria, and sandfly fever in the Pacific and Mediterranean areas, these diseases were frequently listed as the initial impression prior to a final diagnosis of poliomyelitis.

SUMMARY

Data taken from the clinical records of 149 fatal cases of poliomyelitis are analyzed.

The disease is less prevalent in the Army than among the general population, but the mortality among military personnel is higher.

The discussion of the classification of types of the disease and their incidence has been presented.

Symptoms:

a. Duration of symptoms: Ninety-six per cent of the patients were hospitalized within a few days of the onset of symptoms.

b. General symptoms: The temperature was recorded as elevated in 92 per cent of the patients at the time of hospitalization. Headache, stiff neck, and weakness of the extremities occurred in approximately 75 per cent of the cases. Hyperalgesia, involving the back, shoulders, pelvis or extremities occurred in 63 per cent of the cases. Backache occurred in over 50 per cent. Convulsions, lymphadenopathy and dysuria were rare. Skin rashes occurred in only two patients.

c. Gastro-intestinal symptoms: Vomiting, abdominal pain and distention were fairly common symptoms. Constipation was twice as frequent as diarrhea.

d. Repiratory symptoms: Dyspnea and cyanosis were frequently noted. Symptoms simulating an upper respiratory infection were present in approximately 25 per cent of the patients.

e. Genito-urinary symptoms: Urinary retention occurred in 51 per cent of the patients and persisted until death in 38 per cent. The phenomenon was transient in 9 per cent. Incontinence occurred in 3 per cent of the patients.

f. Nervous symptoms: Bulbar symptoms occurred in all except three patients with the encephalitic type of the disease. Of the cranial nerves involved, the tenth was the most frequently affected. Paralysis of deglutition was common and persisted until death in 49 per cent and was transient in only 2 per cent.

g. Paralysis of the extremities: Paralysis of the extremities occurred in 87 per cent of the patients within four days following the onset of symptoms and within one day in 14 per cent. An analysis of the distribution of muscle paralysis and reflex changes has been presented. The cremasteric and abdominal reflexes invariably disappeared as the paralysis ascended from the lower extremities to produce bulbar symptoms.

Laboratory Data:

a. Spinal fluid: The spinal fluid was usually clear. Normal cell counts were observed in 14 per cent of the cases. There was no absolute distinguishing characteristic in comparing the spinal fluid of patients with the pure bulbar type of the disease and that of the patients with the bulbar spinal type. The quantitative protein content was found to be elevated in 85 per cent of the spinal fluid examinations. An increase in the sugar was noted in 55 per cent. There was nothing characteristic in the cases in which the spinal fluid sugar content was high. Normal chloride values were found in 57 per cent. Colloidal gold curves were abnormal (but of no characteristic pattern) in 61 per cent. The Wassermann reaction was found to be positive in only one out of 17 cases in which the test was made.

b. Urine: Urinary findings were those observed in any febrile illness.

c. Serology: A Wassermann test of the blood was made in 17 cases and the reaction was negative in all.

d. Blood sedimentation rate: Sedimentation rate was determined in 23 cases and was found to be normal in 22 per cent and elevated in 78 per cent.

e. Hematology: The leukocyte response has been analyzed.

Mortality, clinical picture, diagnosis and therapeutic measures have been discussed. The short duration of life of patients treated in the respirator (82 per cent of the patients died within three days) has been noted.

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Dangers of Local External Heat and Trauma to Ischemic Tissues in Peripheral Vascular Diseases

Roy J. Popkin, M.D., *Los Angeles*

THE purpose of this article is to refresh the minds of the medical profession regarding the dangers of local heat or trauma to ischemic extremities. Every textbook discussing peripheral vascular diseases mentions the possibility of gangrene, burns or ulcer formation following the application of what normally would be considered safe and therapeutic amounts of heat. Regardless of the method of application, such as diathermy, infrared, electrical cradle, heating pad or hot water bottles, disastrous damage to the tissues might result. Extreme care is necessary.

Likewise, minimal trauma, such as bruising of the tissues or that caused by surgical removal of corns or calluses, or the application of caustic medications such as salicylic acid compounds, might be a source of danger in ischemic limbs.

As the author recently has observed an increasing number of such cases, it was felt that a brief review of the defective heat regulatory mechanism, as well as a discussion of the deficiency in healing of the ischemic tissues, might be timely. These cases are found most frequently in those suffering from arteriosclerosis obliterans, although thromboangiitis obliterans, generalized scleroderma, acute arterial occlusion and injuries to the arteries are frequently encountered. In addition, the decreased cellular activity of aging tissues as found principally in the more elderly arteriosclerotics, is a complicating factor in the healing process.

Ischemic tissues tolerate the local application of heat poorly. The basic principles are physiological and mechanical. These principles are:

1. Heat accumulates more quickly in ischemic tissues. The local heat regulatory mechanism cannot function properly. The normal physiological response to a rise in the environmental temperature of an extremity is an increased blood flow. On the application of external heat the vessels dilate, resulting in an increased flow of fresh blood which carries the heat away. Ordinarily this increased flow carries the locally heated blood to other parts of the body, chiefly to the surface, where the mechanism of radiation and increased perspiration cool it to normal. In the patient with arterial occlusion the increased blood flow is restricted. As a result the heat quickly accumulates in the tissues to dangerous levels.

2. External heat increases the metabolic activity of the cells. More oxygen is required and more waste products are formed. As a result, an increased blood flow is required. This increased demand cannot be met. The cells suffer acutely from the inability of the stenosed or occluded vessels to permit an increased blood flow required by a rise in local environmental temperature. Gangrene frequently supervenes.

3. Ischemic tissues lose their ability to discriminate between dangerous and safe degrees of heat. Nerve structures are very sensitive to a reduction in blood flow. Degenerative changes occur early. The receptor organs for warmth lose their efficiency. A much greater degree of heat is required to stimulate these end organs than would normally be necessary. It is possible for the individual to apply burning degrees of heat to an ischemic extremity without being aware of it.

The reaction of ischemic tissues to injury or infection is likewise affected. Frequently the arterial circulation is so poor that only minimal cellular activity can be maintained. Any additional burden such as that which is required in the healing process of injured or infected tissue cannot be met. This might even be impossible at absolute bed rest. The slightest skin abrasions will result in delayed healing or non-healing. Fungus infections of the toes in the presence of local ischemia are likewise potential sources of non-healing ulcers and gangrene. Caustic preparations for treating ringworm, those containing phenol, benzoic or salicylic acids, are also dangerous. Surgical removal of corns or calluses, or surgical treatment for ingrown toenails, occasionally is followed by serious results. It must also be kept in mind that the process of repair of tissue after injury is altered in the aged. Likewise the resistance of these aging cells to infection is inadequate. This throws an additional burden on an already ischemic tissue.

The following cases which were recently observed are illustrative of the problems involved. The patients were under constant medical care and had been repeatedly cautioned as to the effect of heat, caustics and trauma to the affected extremities.

Case 1.—A 63-year-old man had arteriosclerosis obliterans with diabetes mellitus of many years' duration. The diabetes was well controlled. The blood sugar levels were usually about 100 mg. per 100 cc. The patient had suffered from severe intermittent claudication for the preceding three years. Acute occlusion of the right femoral artery, apparently on an atheromatous basis, had developed about a year previously. This was followed by an ulcer of the dorsum of the foot which required several months to heal. The ischemic symptoms partially subsided. The patient, who was ambulatory, visited a chiropodist who trimmed his toenails, and signs of early infection in a small abrasion alongside the nail of the right big toe followed. In spite of intensive therapy with large doses of penicillin, Tyrothricin solution locally, x-ray therapy locally and absolute bed rest, the infection spread, resulting in a painful ulcer of the distal portion of the toe. The big toe soon became completely gangrenous. Two months after the initial trauma, amputation of the leg below the knee was necessary. The wound healed by primary intention.

Case 2.—The patient, a 60-year-old woman with severe generalized scleroderma, had been under constant observation for over a year, then was lost sight of for five months. On her return she was found to have dry gangrene of the fourth and fifth toes of one foot, with intense pain. She said that she had been under medical care in the interim and that, as her feet were frequently cold, another physician had advised the use of local heat. She then applied an electric pad at low heat. After two or three nights the toes became dark and discolored. The two toes quickly became gangrenous. Within three weeks the distal half of the foot was involved in the gangrenous process. The patient died before surgical operation could be attempted.

Case 3.—The patient, a woman 64 years of age, had arteriosclerosis obliterans with diabetes mellitus. The diabetes, which was of long standing, was well controlled by diet. Moderate intermittent claudication had been complained of for about two years. There was an acute occlusion of the left femoral artery. The ischemic symptoms subsided in about two months. In getting out of bed, the patient struck the affected foot against the metal side, causing a slight abrasion of the dorsum of the middle toe. This showed no indication of healing, although the rest of the foot was in good condition. After three weeks the area of abrasion suddenly started to show signs of discoloration. The entire toe rapidly became gangrenous, to be followed within a week by the adjoining toes. Within three weeks of the flare-up the distal third of the foot was involved and a mid-thigh amputation became necessary.

In reviewing these cases one cannot definitely state that the gangrenous processes were touched off by traumata. However, as progress had been satisfactory in each case until the time of trauma, by heat, impact or caustic medication, it is felt that the gangrene would not have developed spontaneously.

CONCLUSION

Attention is called to the potential dangers of external heat, impact, trauma, infection or caustic medication to ischemic tissues found in peripheral vascular diseases.

2007 Wilshire Boulevard.

Correction

An error was made in a footnote to the article, "The Berman Foreign Body Locator," by J. P. McBride, M.D., which appeared on page 276 of the October issue of California Medicine. The footnote appeared: "The biplane fluoroscope developed by Leishman may also prove to be an additional aid in exact location at the time of operation." It should have been worded: "The stereoscopic fluoroscope developed by Leishman may also prove to be an additional aid in exact location at the time of operation."

CASE REPORTS

◀ Hereditary Angioneurotic Edema: A Remarkable Family History ◀ Charcot's Joint With Secondary Purulent Arthritis Treated With Intra-arterial Penicillin

Hereditary Angioneurotic Edema: A Remarkable Family History

ANNA F. BARNETT, M.D., *Palo Alto*

"I SHALL never forget a case in which my healing art would have proved unavailing and which would have terminated fatally had it not been for the advice of a worthy colleague. The disease was quite new to me in its manifestations and was amazing because of its sudden relapses. I will tell you briefly the whole story because it is to me the strangest of all my medical tales.

"A worthy gentleman, who, as a result of his sober way of living, had attained his 62nd year, awoke one morning with a remarkably puffy face. The lips and eyelids were unbelievably swollen, looking much as if he had been stung by a bee or a wasp. The swelling was lymphatic, without noticeable inflammation, and entirely without pain, burning, or itching. The pulse was natural and the body entirely healthy, though I should not forget to mention that he had suffered every winter from a kind of rheumatic cough from which he always recovered without medical aid.

"But this winter, instead of the usual cough, this strange malady appeared. I ordered the patient to bed and gave him draughts of elderberry tea with liquor anodinus and left the rest to nature. The swelling had completely disappeared by afternoon; it had left the face and descended to the scrotum. The patient felt the arrival there of the new swelling as a brief, sharp sting. Inside of fifteen minutes the whole scrotum was swollen larger than an ox bladder, like a monstrous hydrocele. But there was no burning, pain, or itching; nor were there chills, fever, or thirst. I saw no danger and deemed it a passing acrimony of the humors not yet ripened and ready for transpiration, so I stood fast by the elderberry tea which I had previously ordered and hoped for a healing sweat. I laid cotton soaked in juniper and burnt sugar on the edematous scrotum, and inside of five or six hours the malevolent trouble disappeared and flew to the tongue.

"The tongue could no longer find room in the throat. It swelled out through the lips and filled all who saw it with pity and fear. Now it was time to put other strings to our bow, to employ mightier means against this dangerous fellow. There was good reason to fear that the malicious vagabond might take a notion to invade the windpipe, the lungs, or the brain and cause deadly damage there. Cupping was tried, then blisters, sweats and emulsions of camphor; but the swelling remained stubborn, changing its place every day. Now it was the left, now the right ear, now both; now the eyelids, or the forehead, now the arm. A consultant suggested that the cause of the frequent relapses might be found in the digestive tract. Fortunately, this proved to be the case as the repeated use of tartar emetic alone was able to ban this remarkable and dangerous evil, which, with the continued use of the impotent elderberry tea, might perhaps have killed the patient in spite of his sound heart."

Franz Anton Mai, Professor at Heidelberg, published in 1777 a charming, widely-read book entitled, "Stolpertus, a Young Doctor at the Bedside," which contains this report of a case of angioneurotic edema.[16] The frontispiece woodcuts from the same work show the close association of the doctor of that time with the graveyard, a rare insight in a medical contemporary.



Mannheim
Bei C. F. Schwan, kuhrfürstl. Hofbuchhändler.
1777.



Zweiter Theil.

Mannheim,
bei C. F. Schwan, kurfürstl. Hofbuchhändler.
1778.

The disease may be defined as a transient edema which may involve the skin, mucous membranes, subcutaneous tissue and muscle; usually migratory, one swelling subsiding as another develops. It was well described by Quincke[20] in 1882 under the name of acute circumscribed edema and is often referred to as Quincke's disease or Quincke's edema. Among the other names for it in the early literature are "ephemeral congestive tumors of the skin," "ephemeral cutaneous nodosities," "giant hives," "wandering edema." Recognizing the neurotic element, Strübing[27] first called it "angioneurotic edema" in 1885. Osler,[18] in 1888, published an excellent description of the familial type. The typical swelling may involve a hand, or forearm and hand, or the face or some part of it, the lips and tongue, or the external genitalia, in fact, any part of the body surface. The swelling is usually of a brawny hardness, the border often being sharply demarcated from the adjacent normal tissue. Involvement of the hand makes flexion of the fingers impossible and the member useless. The swellings are deep and may involve skin, subcutaneous tissue and muscle; the skin is glossy and taut and subcutaneous bullae may be present. There is no inflammation.

In addition to the surface swelling, internal organs and tissues may be involved. Swelling of the mucous membranes and of the subjacent tissues is common, particularly in the region of the mouth and larynx. Swellings of the lips and tongue make speaking and eating difficult. Involvement of the larynx may cause partial obstruction with stridor, cyanosis and labored breathing, or complete obstruction with death from asphyxiation. The edema may extend to the bronchial mucosa. However, there is some doubt about the classification of certain cases of transient localized areas of edema of the lungs with roentgenographic findings similar to those of tuberculosis. They are described as visceral manifestations of angioneurotic edema, but should probably be classed as examples of Löffler's syndrome, or as a manifestation of a disseminated visceral angiitis.

Severe cramp-like abdominal pain is a common symptom either accompanying surface swelling, or occurring in persons subject to the disease. The pain may be substernal or epigastric, suggesting swelling of the esophagus or stomach, or there may be generalized or localized abdominal pain, often accompanied by nausea and vomiting, or diarrhea, or both. The vomitus or stools may be grossly bloody and death has occurred in severe attacks.[17] Because the findings resemble so closely those of appendicitis,[22] biliary colic, or perforated peptic ulcer, with localized tenderness, muscle spasm, fever and leukocytosis, operations have been performed during an attack with various interesting findings.

A tense, swollen cecum and first portion of the ascending colon, with considerable retroperitoneal edema, was reported in one case.[22] No abnormality at all may be discovered except for large amounts of free peritoneal fluid.[8] Lundbaek[15] examined a patient gastroscopically during an attack of abdominal pain and found the entire mucous membrane of the stomach succulent in appearance. The folds were broad as if distended, the color deeper red than normal. There were no erosions and no exudate. Reexamination after the attack had subsided showed a normal mucosa. Attacks resembling ureteral colic with hematuria have occurred in this disease. Oliguria may be noted with attacks involving any portion of the body followed by polyuria as the attack subsides. One case of oliguria with angioneurotic edema occurring during pregnancy has been described, with relief obtained by giving theobromine and aminophyllin.[26] The baby born of this mother developed the typical swellings of the disease 56 hours postpartum. Swelling of the uterus and Fallopian tubes may occur.[4] Hydrarthrosis may be a manifestation of the disease.[21]

The nervous system is not immune to attack. A patient with signs of a brain tumor, including choked discs, vomiting and headache, was found at operation to have only edematous brain tissue.[1] He subsequently developed a typical attack of angioneurotic edema and the neurological signs cleared completely. An attack of transient hemiplegia with aphasia is described and certain migraines are believed to be angioneurotic.[1] A remarkable case of relapsing proptosis due to retrobulbar swelling has been reported. Recurring swellings of the eyelids accompanied by iritis with increased ocular tension and great pain occurred in a patient who also had attacks of Menière's disease.[13]

The disease is of two main types, the familial and the sporadic. Unfortunately, this distinction frequently is not made in the literature and some confusion results. The sporadic type, which may be acute or recurrent, is undoubtedly an allergic disease and occurs in persons and families with other allergic manifestations. There is no history in this form of the disease, however, of its occurrence in members of the family through generation after generation. It is common for an isolated attack to occur, or for the attacks to be limited to a period of weeks or months. Rarely they may extend over two or three years. In the familial disease, attacks recur irregularly throughout life. In sporadic cases, hives, a scarletiniform rash, or erythema multiforme may accompany the angioneurotic edema, and pruritus is often very distressing.

In differential diagnosis the following list of diseases with somewhat similar symptoms must be considered: Henoch's or Schönlein's purpura, Osler's erythema group of skin diseases with visceral manifestations, disseminated lupus erythematosus, periarteritis nodosa, Löffler's syndrome, Libman-Sachs disease, and possibly nephrosis.

Pruritus, skin rashes, purpura, arthritis and the other systemic diseases just mentioned are not a part of the familial type of angioneurotic edema. Except for the hazard of death from edema of the glottis, it is a benign disease compatible with long life and good health. Attacks of abdominal pain with nausea and vomiting occur in both forms. A very striking difference between the two is that edema of the glottis is a common cause of death in the familial type, but probably does not occur in the sporadic form, although there may be discomfort and apprehension from swelling in that region. The importance of allergy in the sporadic form is indicated by the many reports of cures by desensitization or by elimination of the allergen. The allergens reported are numerous and curious. Foods and inhalants are common. Rowe[23] reports cures with careful elimination diets. Dorst[5] was successful in certain cases in desensitization with vaccines made from bacteria grown from the intestinal tract as well as from infected nasal sinuses and gallbladders. Drugs are common offenders, the coal tar drugs particularly.[3] Estrogenic substances,[24] chlorine in chlorinated drinking water,[14] and chicle[11] in chewing gum are reported as causes of angioneurotic edema. The disease has followed the use of diphtheria antitoxin and also quinine in the treatment of malaria. There are various precipitating factors in the individual attacks; mild physical trauma, like a bump on the head, may be followed by a swelling starting in the region of the trauma; a tight shoe, a fold in the clothing under the buttocks, are cited as precipitating causes. Exposure to cold or wind may precede attacks. Psychic causes are common; unusual emotion—pleasant or otherwise—undue nervous or physical fatigue, may be factors.

The hereditary factor in the familial type is very striking. Osler[18] in 1888 reported a family of 36 members with the disease occurring in several generations. In 1929 Dunlap and Lemon[7] tabulated 21 families from the literature and added one of their own. In the family here reported the disease extends through four generations. There are eight members, a grandfather, a son and daughter, one grandson

and three granddaughters, all of whom were affected. Two died of edema of the glottis.

Susceptibility to the disease is apparently a Mendelian dominant character without sex linkage (male and female are both affected) and there is usually no skipping of generations. Although the appearance and behavior of the swellings are so strikingly similar to those in the allergenic disease, there is great doubt that allergy is causative in the familial form. Certainly, search for allergens, elimination diets and immunization with vaccines have been futile in the familial type of the disease. Theories regarding the cause or causes of this disease and the pathological physiology of the swellings may be mentioned. Strübing, noting the fact that the disease occurred in high-strung, nervous individuals, thought that there was a disturbance of the nervous control of capillaries with a dilatation and exudation of fluid into the tissues.

Hives can be produced experimentally by injecting eserine, a cholinergic drug. However, direct stimulation of cholinergic nerves will not cause hives, refuting the theory that the psychosomatic influence alone causes anigoneurotic edema. Eserine applied locally causes the cells to liberate "H" substance, which initiates a wheal.[3]

Rowe[23] believes that all cases are allergic in nature. Other investigators, including Drysdale and Piness and Miller,[6] think that the hard, pale, non-itching swelling of the familial type is not due to allergy. Farquharson[9] believes both types have constitutional factors, by virtue of which an urticarial reaction is more easily elicited. He notes that both types occur in nervous, sensitive individuals and both are made worse by the patient's worrying about the condition. Farquharson relies on psychotherapy and stresses the fact that the allergen often cannot be found even in the sporadic cases.

Various blood studies have been carried out on patients during attacks. In some cases, counts of erythrocytes and leukocytes and hemoglobin and differentials may be found to be within normal limits. On the other hand, with abdominal pain especially, a high leukocytosis may occur with or without eosinophilia.[12] One wonders whether the attacks of abdominal pain with eosinophilia should not more properly be classified with the group of diseases included in visceral angiitis. The serum albumin-globulin ratio is said to be increased.[7] Black[2] treated patients with vitamin K on the theory that prothrombin formation might have something to do with the permeability of the capillary wall and that this mechanism might be affected by the administration of vitamin K. He found a good percentage of patients with prolonged prothrombin time and obtained relief of symptoms in many cases. Some patients with normal prothrombin time were also benefited.

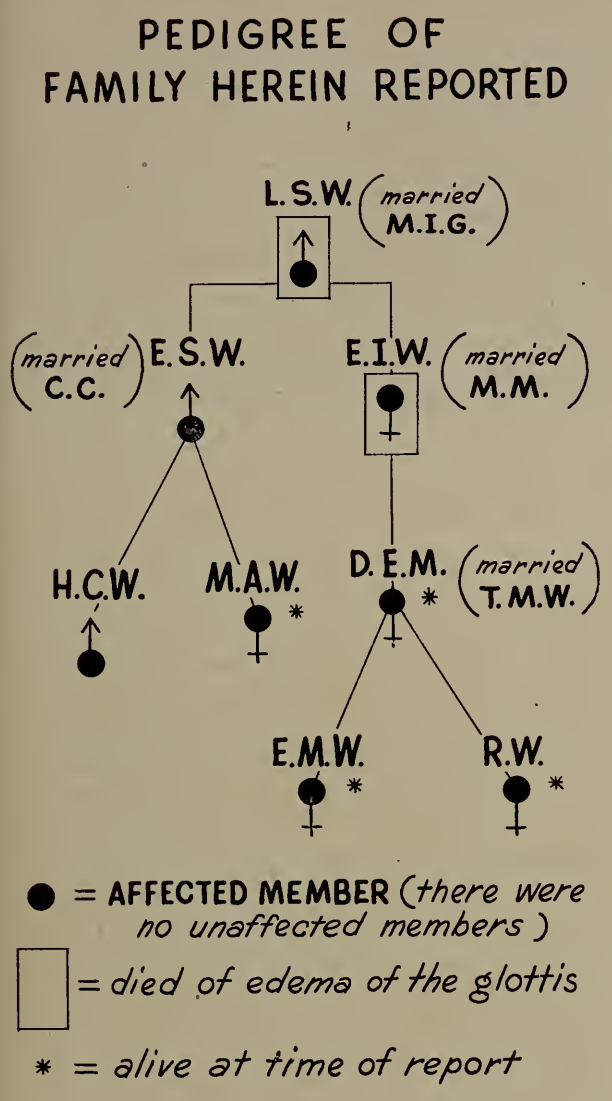
Endocrine dysfunction has been considered a cause of angioneurotic edema. Certainly in the family here reported there are no stigmata of such disorders, and medication with thyroid, parathyroid and ovarian extracts has been of no value.

CASE REPORT

The family here reported is remarkable in that every member was affected. L. S. W. was the first one known to have had the disease, although his mother was thought to have had it. He had two children, E. S. W. and E. I. W., both of whom were affected. L. S. W. died in his twenties from a swelling following a tooth extraction. His son, E. S. W., suffered swellings only occasionally and they became less frequent as he grew older. E. S. W.'s niece remembers one swelling of her uncle's hand caused by the pressure of his thumb over the nozzle of a hose. He died at 47 from another cause. E. S. W. had two children, H. C. W. and M. A. W., both of whom were afflicted. The boy was known to have had one swelling which was thought to have started from the pressure of his watch on his cheek when it slipped down from under his pillow at night. As far as is known, he did not have serious trouble with the swellings. His sister is still alive, quite an old lady, thin and delicate in health. She remembers her first attack—in the throat at the age of 17. She had frequent attacks in her hands and feet during her girlhood. Later, she had only one or two attacks for a period of 13 years, although still later she suffered again from very frequent swellings. She feels that food causes swellings and is also convinced that the swellings are more apt to occur when she is weak and nervous. E. I. W., the daughter of L. S. W., suffered the usual swellings of the extremities and

TABLE 1.—*Tabulation of Cases of Angioneurotic Edema of the Familial Type Collected from the Literature by Dunlap and Lemon in 1929*

	Generations	Members	Members Affected	Deaths	
Osler	6	42	24	2	
Crowder and Crowder	5	64	28	15	
Ricochon	4		9	3	
Schlesinger[25]	4	15	5		
Ensor	5	80	33	12	
Dinkelacher	2	4	3		3rd member reported by Valentin
Strübing	2	4	3		Father, son, daughter
Falcone	3		2		Grandfather and child
Krieger	2		2		Mother and son
Fritz	3	9	8	5	Deaths from edema of glottis
Roy	2		2		Mother and daughter
Yarian	2	15	10	2	One death from edema of glottis
Griffith	2		2	2	Father and patient died from edema of glottis
Harbitz	3		6		
Morris	2		3	1	Death from edema of glottis
Halsted	3		7		
Halsted	2		4		
Halsted	2		3		
Smith	2		2		Mother and daughter
Mendel	4	12	9	6	Deaths from edema of the glottis
d'Appert and Delile	3		5		
Dunlap and Lemon	4	23	11	6	Two died of edema of glottis



had seven or eight attacks in her throat. Once it was thought to have been caused by leaning her forehead against her hymn book in church. The inhalation of steam from boiling vinegar was believed to bring relief. She died at the age of 27, when her daughter, D. M. W., was three months old. She was standing by the stove and fell dead. Autopsy showed death from asphyxiation due to swelling of the larynx.

D. M. W., living in 1947, aged 73, was the source of information regarding her family. Her first attack, she was told, was when she was 3 or 4. She suffered attacks of acute abdominal pain during childhood which were called bilious attacks. The first swelling she remembers occurred when she was 17. It was in her hand or arm and came during a period of illness in the family, when she was anxious and depressed. She had attacks of stomach trouble at this time and frequent swellings of hands and face. She was treated with stomach lavage and iron. Her first prolonged period of migratory swellings occurred during her first pregnancy and lasted ten days. She suffered many swellings in her throat, some of them producing difficulty of breathing and cyanosis. On two occasions, obstruction to breathing was complete and tracheotomy became necessary.

This woman, as can readily be imagined, was constantly haunted by fear of her disease. She suffered from malnutrition at one time, due entirely to a fear of causing a swelling by some food. She was almost entirely free of attacks during the two years her husband was away from home during the first World War, and had a comparatively long period of freedom following a severe attack of measles in adult life. The attacks, except when they involved the digestive tract and throat, were not painful but were usually accompanied by malaise of sufficient degree to cause her to take to her bed.

Her daughters, E. M. W., aged 43, and R. W., aged 42, have the disease in forms similar to their mother's except that they suffer less malaise. Both have had attacks of severe abdominal pain, however, requiring morphine for relief. E. M. W. was operated upon for appendicitis during one attack which resembled that disease closely. There were a leukocytosis of 22,000 with 90 per cent polymorphonuclears, exquisite tenderness at McBurney's point and rebound tenderness. At operation, a normal appendix was found but the peritoneal cavity was full of a pinkish fluid which coagulated instantly on cooling. The patient recovered uneventfully and was absolutely free from swellings for two years after the operation.

R. W.'s story is in most respects similar to her sister's—swellings of extremities and face, and abdominal colic. She had one attack of edema of the glottis necessitating tracheotomy. These sisters, the last of the line, are unmarried.

Attempts at therapy have been numerous and futile. D. E. W. was skin tested, and although she gave positive reactions to certain foods, dust and pollens, elimination diets and immunization to other allergens were of no benefit. Vaccines made from her intestinal flora were tried. The following were used unsuccessfully in treatment of this patient:

Adrenalin	Ephedrine
Pituitrin	Thyroid
Bromides	Vitamin B 1 and B 6
Chloral	Ultraviolet rays
Atropine	Soda
Pilocarpine	Autogenous vaccine from intestinal flora
Histamine	
Benadryl	Parathormone
Ovarian extract	Gynergen
Aspirin	Activin
Morphine	Torantil
Calcium lactate	Pyribenzamine

Those that were suggested but not tried were insulin, bee venom, autogenous blood, horse serum, Vitamin K, and x-ray.

300 Homer Avenue.

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Charcot's Joint With Secondary Purulent Arthritis Treated With Intra-arterial Penicillin

John Ordie Shaffer, M.D., *Minneapolis*

SECONDARILY infected tertiary syphilitic lesions are frequently equally resistant to anti-syphilitic measures with either the heavy metals or antibiotics and present a difficult therapeutic problem. A standard treatment by arsenicals or bismuth is ineffectual because of the superimposed bacterial infection, and although penicillin may be effective against the particular infecting bacteria and also treponemacidal, it may fail when administered intramuscularly or intravenously because of the poor permeation into the involved region. Local factors of impaired vascularity and fibro-osseous barriers prevent penicillin from gaining entrance into the involved area when the drug is administered by the intramuscular or intravenous methods; but, fortunately, by the intra-arterial route it is possible to overcome these barriers and thus achieve the desired therapeutic result. The following case report illustrates that after the failure of intramuscular penicillin therapy of a secondarily infected syphilitic lesion a prompt desirable result attended treatment with smaller dosages of penicillin given by the intra-arterial route.

From the Surgical Service of Owen H. Wangensteen, M.D., University of Minnesota Hospital.

CASE REPORT

The patient, a man 64 years of age, had had swelling and purulent drainage from his left foot over a ten-year period (1935-1945) and had been incapacitated because of it many times. Since May, 1945, there had been an exacerbation of symptoms and he was finally admitted to a hospital in mid-August, 1945, and given a six-day course of 20,000 units of penicillin intramuscularly every three hours (160,000 units daily). This had no effect on the swelling or purulent drainage and both conditions continued to increase in severity. On referral of the patient to the University of Minnesota Hospital on 27 September, 1945, physical examination revealed a small, thin, fairly well developed man with a temperature of 102° F. and a pulse rate of 100 per minute. There were erythema and edema of the medial distal one-half of the left foot and two indurated purulent draining sinuses on the plantar surface of the first metatarsal of the foot. A moderate edema of the left leg extended up to the knee and an enlarged tender left inguinal node was palpated in the groin. The blood pressure was 165 mm. of mercury systolic and 68 mm. diastolic, but the heart was otherwise normal, as were the lungs.

Neurological examination of the patient revealed that the pupils reacted sluggishly to light but normally to accommodation. Anisocoria was present, with the right pupil larger than the left. Knee jerks and ankle jerks were diminished and posterior spinal column disease was further evidenced by a positive Rhomberg test, decreased muscle, tendon, joint, and testicular pain, and decreased sense of vibration and position in the lower extremities. Superficial sensation was intact. As to mental status the patient was of normal intelligence with no gross abnormalities. Venereal history was denied but a clinical diagnosis of tabes dorsalis with Charcot's joint of the foot was confirmed by a neuropsychiatric consultant. Laboratory studies revealed a hemoglobin of 10.4 gm. and a leukocyte count of 13,850 per cubic millimeter with a differential count of 84% neutrophiles and 16% lymphocytes. The blood sedimentation rate was 120 mm. in 60 minutes (Westergen). Blood chemistry determinations, including fasting blood sugar, were within normal limits. Upon urinalysis a trace of albumin and an occasional cast were found. A culture of the purulent exudate from the foot revealed coagulase-positive staphylococcus aureus to be present. Results of initial serological tests for syphilis were: Kline, doubtful; Hinton, doubtful; Kahn, negative. Subsequently, reactions to the Kolmer test were negative, to the Kline test 2+, and to the Eagle test 3+. The spinal fluid cell count was normal (2 cells per cubic millimeter) but the protein was elevated to 304 milligrams per 100 cc. A first zone colloidal gold curve was present but results of spinal serology were negative. A roentgenogram of the foot (Figure 1) showed a destruction of the first metatarsophalangeal joint with considerable fragmentation and new bone formation in the soft tissues characteristic of Charcot's joint with probable secondary purulent arthritis present.

Intra-arterial injections of 50,000 units of penicillin were given into the femoral artery twice daily over a five-day period until a total of nine injections had been given. The penicillin was diluted in 10 cc. of normal saline and given into the femoral artery in a perpendicular plane using a 10 cc. syringe and a 20-gauge two and one-half inch needle. A blood pressure cuff was placed on the left thigh and inflated to 80 mm. of mercury prior to the intra-arterial injection and maintained at that pressure for ten minutes following each injection. Foot soaks of potassium permanganate solution (1:9000 concentration) were used twice daily as a therapeutic adjunct. The cellulitis cleared entirely in 48 hours and drainage ceased in 72 hours. Following intra-arterial penicillin therapy a sterile dressing was applied to the foot and the skin had entirely grown over the sinus tracts



Figure 1.—X-ray of left foot revealing destruction of the first metatarso-phalangeal joint and new bone formation in the soft tissues characteristic of a Charcot's joint.



Figure 2.—X-ray revealing increase in density at first metatarso-phalangeal joint and no evidence of residual infection five months after hospital discharge.

within two weeks of the start of therapy. The patient was able to walk on the foot without difficulty following this and was discharged from the hospital on 24 October, 1945. A roentgenogram of the foot (Figure 2) taken 6 March, 1946, showed an increase in the density in the bone in the involved area at the first metatarso-phalangeal joint. There was no evidence of residual infection in the foot. The patient was followed by the neuropsychiatric clinic concerning the tabes dorsalis but had had no further difficulty with the left foot when seen one year after hospital discharge.

COMMENT

In a generalized infection without abscesses (septicemia) the determining factor of successful penicillin treatment is the effective bacteriostatic level of penicillin required in the serum as determined by the penicillin sensitivity of the infecting organism, but in a local area of suppuration (abscess) in an extremity, the permeability of the wall of the cavity is the more important since fortunately most of the bacteria found in infections of the extremities are sensitive to penicillin.[2]

Thus, in septicemia, penicillin may be given in the required dosage by the usual intramuscular or intravenous routes depending upon the sensitivity of the organism. However, in abscesses even a high concentration of penicillin in the serum may be ineffectual and the method of administration must be altered so as to obtain an effective penicillin concentration locally within the abscess. In many infections of the extremities the large area involved and the presence of multiple fascial and bony pockets have made local injection untenable but fortunately intra-arterial penicillin has been found to be efficacious in these cases. In addition the use of a blood pressure cuff placed just about the knee and inflated to a subdiastolic pressure (80 mm. mercury) prior to the intra-arterial injection and for the 10 minutes following, obstructs the venous return but permits the systolic pressure to force the concentrated drug into the local area supplied by the artery without significantly increasing the dilution of the drug.

The comparative efficacy of the intravenous and intra-arterial methods was borne out by an experimental study using radioactive phosphorus (P_{32}) and a Geiger counter for tracing in a series of normal subjects.[1] These studies revealed that every determination in the toes, dorsum of the feet, and midcalf of normal subjects, who were given radioactive phosphorus intra-arterially with a proximally placed blood pressure cuff inflated to 80 millimeters of mercury for stasis, was over the intravenous mean value for a period of three hours. This indicates that this intra-arterial method gives a higher concentration in the leg than the intravenous method during this time. For the first hour the mean Geiger counts of the determinations done on the toes and dorsum of the feet were over twice the values later determined by intravenous injection in the same subjects. Maximal values obtained with intra-arterial injection and a blood pressure cuff for stasis remained over twice the maximal values obtained by intra-arterial injection without a cuff for a period of 30 minutes and did not fall to the level of maximum values without a stasis cuff for one and one-half hours, indicating the stasis cuff permits a higher concentration than the simple intra-arterial injection for one and one-half hours. With the stasis cuff at 280 millimeters of mercury minimum values were occasionally below the mean for the intravenous method for the initial 30 minutes, indicating that the radioactive phosphorus may be withheld during this time and suggesting that the stasis cuff at 80 millimeters of mercury gives more consistent results.

Since the method of administration of penicillin is a more important variable than the dosage of penicillin, the therapeutic result in the case herein reported was better from a small dosage of penicillin given intra-arterially than was obtained from a larger dosage of penicillin given intramuscularly. The simple technique of intra-arterial injection has previously been described elsewhere and its safety is exemplified by a previously reported case of a 70-year-old woman who received a total of 30 intra-arterial injections at approximately the same site in the common femoral artery over a period of 16 days without hematoma formation or any other difficulty.[2] The present case is presented as an example of the efficacy of penicillin given intra-arterially.

SUMMARY

1. A report of a case is presented in which a patient with a secondarily infected Charcot's joint of the foot was not benefited by penicillin given intramuscularly but experienced good results later when a smaller amount of the drug was given intra-arterially.

2. Intra-arterial injection of penicillin is suggested for the treatment of secondarily infected syphilitic lesions of the extremities.

Minneapolis General Hospital Doctors' Residence.

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CLINICAL SYMPOSIUM

Prepared under the direction of EDGAR WAYBURN, M.D., *San Francisco*, and CLARENCE J. BERNE, M.D., *Los Angeles*

The Management of Peripheral Vascular Insufficiency In Arteriosclerosis Obliterans

PATHOLOGY: DR. BENJAMIN E. KONWALER*

The arterial changes which occur from infancy to old age, without apparent disease, are well known. These comprise thickening and reduplication of the internal elastic membrane, calcification of the media, and may include fatty infiltration and hyaline degeneration. It is not entirely obvious which of these changes are physiologic and which are pathologic. However, the evidence is strong that arteriosclerosis may be, in part, not only pathologic but even reversible. Thus lipemia, hypertension, and diabetes mellitus may accelerate the progress of arteriosclerosis, while wasting disease may effect a reversal of the process.

Arteriosclerosis obliterans of the peripheral arteries is clinically considered to be part of a generalized condition associated with old age. However, the histological foundation for its development may appear as early as the first decade of life.

In the non-diabetic person, the arterial change seen in the muscular vessels of the extremities is predominantly the Monckeberg type of sclerosis with medial calcification. This lesion is distinct from the atheromatous process which may be encountered in elastic vessels, such as the aorta. There is little, if any, relationship between the medial type of arteriosclerosis and the atheromatous. Furthermore, the degree of involvement of different muscular arteries in any one patient is far from uniform, so that there is no necessary association of advanced arteriosclerosis of the extremities with a comparable process in the arteries of the heart, of the kidneys or of other regions.

If the pathologic changes remain limited to the media, the lumen remains intact or may even be widened. When, however, the intima is involved, then the lumen is narrowed. In some cases, ulceration of the endothelium occurs, and is followed by thrombosis. Calcification or other degenerative changes in the walls of the arteries do not, in themselves, cause symptoms. It is when occlusive thrombosis occurs that symptoms develop.

In diabetic individuals the atheromatous type of lesion is the outstanding one, even in the muscular arteries, where it may occur alone or superimposed upon medial calcification. As a result the obliterative process not only tends to become apparent at a relatively early age, but there is likely to be an extensive involvement of small vessels so that compensatory development of a collateral circulation may be poor.

In contrast to thromboangiitis obliterans (Buerger's disease) arteriosclerosis is localized in the arteries themselves whereas in thromboangiitis obliterans the inflammatory process extends beyond the arteries to the accompanying veins and nerves. In arteriosclerosis obliterans, phlebitis and periarterial neuritis are not usually seen.

SYMPTOMS: DR. DONALD W. LEIK†

The first evidence of deficient circulation in an extremity is likely to be pain brought on by the use of that extremity. If the legs are involved and the individual steps out, he fails to obtain a sufficient blood supply for his laboring muscles, rests and sets out again, suffering in fact the intermittent claudication first described over a century ago in the case of the horse, by French veterinarians. Characteristically the pain is cramp-like and is felt in the calf, but variations from the usual picture are not uncommon. The affected region may be the sole of the foot, the instep, even the thigh. The complaint may be a dull ache or numbness. Moreover, in the upper extremity weakness may be more frequently the complaint than pain. Recognition of intermittent claudication is based on the relation to exercise. Any uncomfortable sensation in an extremity which is brought on by exercise and relieved by rest is intermittent claudication. It is angina of the legs. By contrast the pain of flat feet, or of venous stasis is worse when the patient stands still than when he walks about, whereas intermittent claudication is relieved by standing still. The pain of arthritis does not cease until the patient sits down.

The arteriosclerotic patient may describe another type of pain, one which comes on at night and awakens him out of sleep. This is probably the result of local ischemia which occurs when the systemic circulation is slowed during sleep. Relief is obtained by placing the painful extremities in a dependent position. Idiopathic nocturnal cramps may often be distinguished from the rest pain of arterial deficiency by giving the patient a single capsule of quinine before bedtime. This may relieve cramps but will not affect the pain of arterial deficiency.

Persistent, continuous pain in the extremities, especially in the toes and forefoot, may be the forerunner of impending gangrene. If such a pain appears suddenly, it usually signifies thrombosis of a major artery, and prompt treatment is called for.

Some patients may complain of coldness or blueness of the extremities. These symptoms are more likely to signify spasm of the vessels than organic

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From Birmingham Veterans Administration Hospital, Van Nuys, California.

* Chief of Laboratory Service.

† Chief of Cardiovascular Section.

occlusion. However, an association of vasospasm with arterial occlusion is not uncommon especially after a fairly recent thrombosis.

Physical Signs

The examination of the patient should be performed in good natural light at a comfortable room temperature. In starting the examination the physician should note atrophy of the skin or trophic changes in the nails. Hairless atrophic skin on the lower legs is frequently seen in arteriosclerosis obliterans. Skin color on the sole and dorsum of the foot should be observed in three leg positions: horizontal, elevated to an angle of 45 degrees, and dependent. Pallor may develop only after the legs have been elevated for two or three minutes and may be overlooked if the period of elevation is too brief. An excellent measure of inflow rate, which can be recorded accurately, is the time, in seconds, required for color return when the feet are placed in dependency from an elevated position. The characteristic dependent rubor of arterial insufficiency likewise requires several minutes for its full development.

Ulceration is not a rare result of arterial insufficiency. It tends to occur distal to the malleoli, in contrast to the ulcers of venous stasis which usually appear in more proximal tissues. In most instances these ulcers are exquisitely painful so that local treatment is difficult. At other times, in diabetic patients especially, one may be surprised to find almost no discomfort associated with a deep ugly-looking sore. Too often an ulcer on a toe due to arterial insufficiency is mistaken for an ingrown toenail.

Adequate examination should include not only palpation of the dorsalis pedis and posterior tibial pulses, but also the popliteal, femoral, radial, and ulnar pulses. Unfortunately, palpation of the arteries in the lower extremities is not part of most routine physical examinations. Yet, unless one is thoroughly familiar with the exact location of the normal pulses, it is impossible properly to interpret the apparent absence of pulsation in a suspected case of arterial insufficiency. Approximately ten per cent of normal individuals will exhibit a bilateral absence of the dorsalis pedis artery. Unilateral absence of the latter is suggestive of arterial disease, and absence of any of the other lower extremity pulses is definitely evidence of obliterative vascular disease.

The skin temperature can be estimated with the back of one's hand. In this way small differences in comparable areas may be detected and should be observed from the tips of the toes to the knees. Cold toes from which the temperature rises sharply toward the ankle or lower leg are more often associated with vasospasm than with arterial occlusive disease. One may even find relatively warm toes in a patient with no palpable arterial pulsation below the umbilicus. Finally, in examining a patient with peripheral arterial disease, a clinical estimate can be made of the degree of vasomotor activity. An individual with blue, moist, cold skin under which the superficial veins are constricted, has high vasomotor tone. If the skin is pink, dry and warm with prominent superficial veins, the vasomotor tone is low. With marked vasospasm the pulses about the ankle may be difficult to palpate but such active vasospasm may be relieved by immersing one or two of the other extremities in warm water at 110° F. for a maximum of 35 minutes.

From the viewpoint of prognosis rather than of therapy, it is desirable to determine whether peripheral vascular occlusion is due to thromboangiitis obliterans or arteriosclerosis obliterans, and if the latter, if it is associated with diabetes mellitus. Inasmuch as mild diabetes may not produce glycosuria, blood sugar studies should be performed in the presence of arteriosclerosis obliterans in individuals under 60.

The following table lists some of the criteria by which arteriosclerosis obliterans may be distinguished from thromboangiitis obliterans:

	Thromboangiitis Obliterans	Arteriosclerosis Obliterans
Onset	Rarely after 40	Rarely before 40
Sex	99% males	75% males
Upper extremity involvement	40% of cases	Rare
Migratory phlebitis	40% of cases	Never
X-ray evidence of calcification in arteries	None	Frequent

Prognosis

While arteriosclerosis obliterans tends to become progressively more severe, the progress is not uniform in rate, but rather seems to consist of a series of occlusive episodes often due to thromboses. Between these relatively acute episodes the patient's condition may remain static or even show improvement as collateral channels develop. However, at any time, even in the non-diabetic patient, a local infection arising in the poorly nourished tissues of the foot may precipitate gangrene. As a consequence, the therapy of this condition attempts to achieve two objectives: (a) Protection of the ischemic tissues from injury and infection; (b) measures to aid the development of collateral circulation. For a properly treated cooperative patient the outlook for survival of the affected extremities is good. In fact most of these patients will die from other manifestations of their arteriosclerosis, such as coronary occlusion or cerebral hemorrhage, without prior loss of an extremity.

MANAGEMENT: Dr. Theodore B. Massell‡

Personal Hygiene

The first problem in therapy is the regulation of his personal habits by the patient himself. From the beginning he must give up smoking. The weight of recent evidence is against the efficacy of such compromises as cutting down the daily cigarette ration, using denicotinized tobacco or filtered cigarette holders. A complete and permanent renunciation is necessary.

Dietary regulation is also indicated. A low cholesterol diet may slow the arteriosclerotic process and perhaps even cause some reversal in those individuals who manifest a hypercholesterinemia. For obese patients the low cholesterol diet may be included in a

‡ Chief of Vascular Surgery Section.

weight reducing regime. Most patients will understand the desirability of reducing the load to be borne by legs in which the circulation is impaired.

Good foot hygiene should become a habit. The feet should be bathed daily with mild soap and lukewarm water. Drying should be gentle but thorough, especially between the toes, and in these locations wisps of lamb's wool should be placed to prevent maceration. The patient should be taught to cut his nails straight across in a good light. In the older age group in whom vision may be impaired, the trimming of toenails should be done by a younger member of the family or a chiropodist. The services of the latter may be utilized also for shaving corns and calluses which might otherwise provide a source of fissures and ulcers. Trichophytosis should be rigidly controlled.

Both patient and physician must realize that extremes of temperature are to be avoided. Usually the discomfort experienced on exposure to cold results in the assumption of adequate protective clothing by victims of arteriosclerosis obliterans. Wool socks may well be worn year round and in cold climates fleece-lined shoes are advisable in the winter. On the other hand the danger of exposure to heat is too frequently not recognized. In a limb in which there is arterial stoppage the circulation may be just adequate to supply the metabolic needs of the distal tissues at a low level of activity. External heat causes a local increase in metabolic activity of the heated tissues, an increase which cannot be met by more blood flow through the already narrowed or obstructed arteries. The result of the disparity between blood need and blood supply may be gangrene. Consequently the physician must not only avoid the use of local heat (e.g. diathermy, infra-red, hot baths) in treating peripheral arterial disease, but he must warn the patient against self-treatment along that line.

Most patients soon learn from the pain occasioned by exercise that much activity is undesirable when the blood supply is inadequate. On the other hand mild exercise tends to stimulate the development of collateral circulation. Position also may affect the flow of blood into a limb in which the arteries are occluded. The night pain which disturbs the sleep of some victims of peripheral vascular disease may be relieved by the simple expedient of raising the head of the bed on blocks. On the other hand a victim of peripheral arteriosclerosis may develop gangrene merely because his physician treats a mild foot infection by elevating his leg on pillows.

Physical Therapy

It has long seemed plausible to treat peripheral arterial insufficiency by some form of physical therapy. Many ingenious types of apparatus have been devised for this purpose but the results on the whole have been disappointing. One of the oldest mechanical devices to improve circulation is the pressure suction (Paevex) boot. Despite the ingenious theory on which the machine is based, it seems to be ineffective.

Somewhat more recent is the intermittent venous occlusion apparatus or Burdick machine. Its purpose is to produce temporary intermittent obstruction to the venous outflow with the expectation that thereby the blood which flows into the extremity will be more efficiently utilized. In the intact limb reflex vasospasm probably nullifies the action of the passive vascular exerciser, but it may well be of some value when used on a sympathectomized extremity.

The effect of gravity on peripheral blood flow has long been the basis of Buerger's exercises. Unfortunately a patient would have to perform these exercises for many hours each day in order to derive any significant benefit. This routine is likely to be unacceptable even to those rare patients who might possess sufficient physical endurance for such therapy. With an oscillating bed the same effect may be obtained for 24 hours daily without any expenditure of energy by the patient other than that required to secure the money necessary to purchase or rent the bed. Even the ambulatory patient who is occupied by day, may derive benefit from sleeping in an oscillating bed.

Various ways of bringing heat to the body are used in physical medicine. For reasons already stated the local application of heating devices to the ischemic extremities is contraindicated. Heating other parts of the body will bring about a reflex vasodilation in the diseased regions. The limitations of vasodilator physical therapy will be considered with the vasodilator drugs.

Drugs

Physician and patient alike have long been hoping that some drug will be found to relieve the victims of peripheral arterial insufficiency. Too often this popular interest has led to flamboyant articles in the lay press in which bombastic claims for some newly developed medicine may even precede the reports in the medical literature. It is difficult for the physician to maintain his normal scepticism when he is confronted by an enthusiastic patient armed with an authoritative article on some new miracle drug taken from a digest magazine or the daily paper. Actually drug therapy has to date been the least effective form of treatment for peripheral vascular disease.

The majority of the drugs used have been vasodilators. These vary in efficiency but all have certain defects in common.

1. Any form of treatment which produces generalized vasodilation will have more effect in those parts in which there is no occlusive arterial disease than in extremities in which there is considerable obstruction to normal blood flow. So much blood is diverted to normal regions that relatively slight improvement occurs in the circulation of the arteriosclerotic parts. It has been well demonstrated that general vasodilation is much less effective than local vasodilation (as would result from sympathetic ganglion block) in increasing blood flow in an extremity with arterial disease.

2. The local circulatory improvement brought about by vasodilator drugs (or by physical therapy) is of brief duration so that the administration of the drug has to be repeated frequently and continued indefinitely.

3. When surgical sympathectomy has already been performed for peripheral arterial insufficiency, it has been demonstrated that the administration of a generalized vasodilator will cause a decrease and not an increase in blood flow through the sympathectomized extremity.

Despite their lack of therapeutic usefulness the catalog of vasodilator drugs is a long one. Two of the most recent additions are Etamon (tetraethylammonium chloride) and Priscol (benzazoline hydrochloride). A therapeutic dose of either of these is almost as effective as having the patient immerse his arms in warm water for 20 to 30 minutes. Farther down on the list are Padutin (vascormone), Depropanex (deproteinated pancreatic extract), nicotinic acid, and intravenous ether. These differ in the physiologic mechanism whereby they act, but have in common a lack of therapeutic effect. One of the most publicized of the vasodilator drugs is histamine, given as histidine and ascorbic acid. The lack of improvement which has been observed following this form of treatment could well have been predicted, since the dependent rubor of arterial insufficiency is the result of an excess of histamine (or a related substance) already in the poorly nourished tissues. If one wishes to use some vasodilator drug for arteriosclerosis obliterans, an ounce of alcohol by mouth three times a day is probably the best choice. Whiskey is a rather effective vasodilator of fairly sustained action, is not as expensive in therapeutic doses as most other vasodilator drugs, and to many patients it may even be enjoyable.

Other drugs have been suggested for the treatment of circulatory deficiency in the extremities which are not vasodilators, but which purport to alter the properties of the blood or the tissues. These include such remedies as tocopherol (vitamin E), sodium tetrathionate (tetrathione) and cytochrome C. Each has been announced with enthusiasm by its originator but there has been a dearth of confirmatory reports by subsequent observers.

Surgical Treatment

Within the last decade there has been a growing realization that arteriosclerosis obliterans may often be improved by the permanent release of vasoconstrictor impulses such as that which follows surgical sympathectomy. The persistent dilation of blood vessels which results from sympathetic nerve section seems to be a stimulant to the development of new collateral channels.

The injection of procaine into the sympathetic ganglia once or repeatedly does not duplicate the therapeutic effect of surgical sympathectomy, but a single procaine sympathetic block is a diagnostic procedure from which one can derive an approximate idea of the response to be obtained from a permanent sympathetic denervation. If a sympathetic block will relieve ischemic pain, increase a patient's tolerance for exercise, or convert a cold blue foot into a warm pink one, sympathectomy is indicated. Occasionally one may encounter a patient with low vasomotor tone who shows no apparent improvement in circulation following sympathetic block. Such a patient may be made worse by sympathectomy. Neither diabetes nor coronary artery disease is a contraindication for this operative procedure.

The injection of alcohol into the sympathetic ganglia is rarely justified as a substitute for sympathectomy because of the frequency with which the former is followed by neuralgia, paralysis or sloughing. In an emergency in which a sustained vasomotor paralysis is needed for a patient who is too sick to withstand operation, ten cubic centimeters of bromsalizol may be injected safely into the sympathetic ganglia to produce a block which lasts up to a fortnight.

Sympathectomy for arteriosclerosis obliterans should include the first lumbar ganglion as well as those below it. The sterility that usually follows bilateral loss of the first lumbar ganglion in the male is usually no problem in patients of this age group. On the other hand the chief source of arterial blood flow to the leg may be from collaterals which originate from the profunda femoris artery. These receive most of their vasomotor supply from the uppermost part of the lumbar chain. Lumbar sympathectomy does not contribute at all to impotence.

Another useful form of surgical therapy in peripheral arterial disease is local amputation of a toe. When a patient exhibits a chronic ulcer of a toe, perhaps with osteomyelitis of a phalanx, which does not respond to conservative management, it is advantageous to remove the entire toe through the metatarsal head. When the circulation is good at the operative site, the use of modern antibiotics permits a closed amputation. If there is doubt about the local circulation, an open operation is safer, with beveling of the wound to provide good drainage. Articular cartilage should never be left in place at the site of amputation.

In recent years the ligation of veins, such as the femoral or popliteal, has been pretty much discarded as a method of treating peripheral arterial insufficiency. It is now generally conceded that obstructing the outflow of tissue metabolites is rather illogical therapy for a condition in which most of the symptoms are due to an overaccumulation of these metabolites. Furthermore the edema that often follows ligation of a major vein may provide considerable embarrassment to the tenuous collateral circulation.

SUMMARY

Arteriosclerosis obliterans is the result of a common and more or less unpredictable pathological process, the end result of which is frequently occlusion of the arteries by thrombosis. The symptoms and signs are sufficiently characteristic so that the diagnosis can usually be established without any special equipment.

Treatment is symptomatic. The most important factors in good management are the regulation of the patient's personal habits and the proper use of such surgical procedures as sympathectomy and local amputation. Drug therapy is essentially of no value and physiotherapy is of only slight benefit.

Clinical-Pathological Conference

A white American bellboy, 50 years old, entered the hospital on January 2, 1948, with sore throat of nine days' duration.

The patient has always lived in the United States except for a seven-month trip to Alaska in 1943. He said that he consumed a moderate amount of alcohol. A brother had died of tuberculosis.

Present Illness: The patient was feeling well on December 1, 1947, when he went on a vacation to Blue Lake in Northern California. There he drank some raw milk. A few days later a head cold developed and it persisted. On December 25, 1947, after returning to San Francisco, he noticed a sore throat and began coughing up small amounts of white phlegm. These symptoms increased and he went to bed because of chilly feelings, headache, malaise, and generalized aching. The cough became productive of about two cups of white material daily. At the same time there were slight dyspnea and mild anterior chest pain. On December 28 diarrhea developed, with five to seven loose brownish-black stools daily, and mid-abdominal cramps. The patient ate little and lost about 15 pounds.

Although well developed, the patient was thin and appeared to be exhausted. He coughed intermittently. The temperature was 103° F., the pulse rate was 130, and respirations 32 per minute. Blood pressure was 100 mm. of mercury systolic and 65 mm. diastolic. The skin was warm and moist. The nasal mucosa was inflamed, with crusted exudate, and the soft palate and pharynx were highly injected and edematous. No abnormalities were found in the neck, and the lungs were clear to percussion and auscultation. The heart was not enlarged and the rhythm was regular. A soft systolic blowing murmur was heard along the left sternal border. The abdomen was soft and non-tender, and a soft, non-tender liver edge was felt 3 cm. below the right costal margin. There were no abnormalities in the extremities.

Examination of the blood showed a value for hemoglobin of 13 gm. per 100 cc. Erythrocytes numbered 4.2 million and leukocytes 4,500 with 34 per cent polymorphonuclear cells (26 per cent segmented and 8 per cent non-segmented), 60 per cent lymphocytes and 6 per cent monocytes. Corrected erythrocyte sedimentation rate was 24 mm. in one hour. The urine was normal. Results of a Wassermann test were negative. There was no growth on four blood cultures. Alpha streptococci and non-hemolytic staphylococci were identified in a smear from the throat. Studies of the blood for viruses, cold and heterophile agglutinins were negative, as were results of all agglutination tests. The feces were watery, green-yellow. No ova or parasites were seen in stool specimens either in the hospital laboratory or in the health department laboratory. A stool culture grew no abnormal organisms. Nothing of note was found in the sputum which was examined unstained and stained by both Gram and Ziehl-Neelsen methods. A roentgenogram of the chest showed no abnormality.

Course: The fever varied from 100.6° to 103° F. and the patient weakened progressively. Several loose green stools were passed but the main complaint continued to be sore throat. On January 9, leukocytes numbered 22,000, with 78 per cent polymorphonuclear cells (63 per cent segmented and 15 per cent non-segmented). Penicillin was given without apparent benefit. Repeat agglutinations done January 13, 1948, were positive for typhoid in a dilution of 1:80, but agglutinations the next day again were negative. On January 14, the patient complained of abdominal pain and that evening appeared much worse, with a pulse rate of 144 and no blood pressure reading obtainable. There was tenderness and guarding in the left lower quadrant which soon spread to the entire abdomen, with rebound tenderness. Peristalsis remained active. The blood pressure rose briefly to 90 mm. of mercury systolic and 50 mm. diastolic following intravenous injection of blood and fluids, but it soon fell again and the patient died on the morning of January 15.

From the San Francisco Hospital, May 11, 1948.

CLINICAL DISCUSSION

DR. EDGAR WAYBURN*: The course of illness in this patient may be divided into three major phases. The first begins early in December and lasts through most of that month. The chief symptoms are those of a systemic disease, presumably an infection (headache, malaise, chilly feeling, generalized aching), with partial localization to the respiratory tract as shown by the cough productive of as much as two cups of white sputum daily, dyspnea and chest pain. The second phase is revealed and spotlighted by the statement that on December 28 mid-abdominal cramps began, with diarrhea of five to seven loose brownish black stools daily. Shortly after this the patient entered the hospital. At this time he appeared rather severely ill for one who had developed symptoms less than a month before. The physical signs that he had lost a good deal of weight and was dehydrated and exhausted, offer no localizing clues. The laboratory data indicate that the staff was diligent and suspicious of a variety of conditions, and, further, that it was forestalled in its wide search by running into a number of dead-end negative tests.

At this point we may consider the various diagnostic possibilities, as they must have appeared to the attending staff, and where they seem to lead. We are confronted by a severe, subacute to chronic disease which appears to be advancing rapidly and which seems to have attacked both the respiratory and gastro-intestinal systems. The straw man which must be set up in diagnosis is typhoid fever. The onset and the course, the involvement of the respiratory as well as the gastro-intestinal tract are not unfamiliar. The low leukocyte count with a low per-

*Assistant Clinical Professor of Medicine, Stanford University School of Medicine.

centage of neutrophiles in the smear is an ancillary sign of value, as is the appearance of the stool. However, all of the confirmatory tests were negative repeatedly—the blood cultures, the stool cultures and the agglutination tests. (An agglutination test positive for typhoid in 1:80 dilution is without significance, particularly when others are completely negative before and afterward.)

The second disease to consider is tuberculosis, which may very well attack both the respiratory and gastro-intestinal tracts, as this disease did. Here again, all of the laboratory studies negate the historical data: The sputum and the roentgenogram of the chest are the two most important studies here. (In passing, one wonders how the patient could have so much cough, chest pain and sputum and still have a normal appearing roentgenogram of the chest as well as absence of physical signs.)

The third disease which deserves major consideration is amebiasis. The manifestations of amebiasis are protean and the symptoms may be respiratory as well as intestinal. There is nothing in the history or the physical signs of this patient which may not be caused by amebiasis. The laboratory test which could make the diagnosis—the microscopic examination of the feces—is negative, but amebae are all too often not demonstrated, even when special effort is made to find them.

Other conditions which one may consider are systemic fungus infection and regional ileitis, but neither appears very likely. Mention of the fact that raw milk was drunk reminds us that infected raw milk may cause brucellosis as well as typhoid, but brucellosis also appears unlikely.

The third phase of this patient's course began January 9, at which time the leukocyte count was 22,000 with 78 per cent polymorphonuclear neutrophiles. We presume that the blood examination was done at this time because of some change in the clinical status, although there is no mention of it. Whatever the change was, it caused the attending physician to administer penicillin, without apparent effect. Five days later, on January 14, the patient developed signs which suggest perforation of a viscus—or perhaps hemorrhage—followed by shock and peritonitis.

Whatever may be the primary diagnosis, I believe that we have the right to state that the terminal episode, the immediate cause of death, was perforation, probably of the intestine, followed by peritonitis.

To return to the primary diagnosis, we have a condition which has progressed rapidly and lethally over a known period of five weeks and which has involved the intestine in an ulcerative process which ends in perforation. I think that we may rule out tuberculosis first, for in order to have tuberculous enterocolitis of this severity and nature the patient would almost have to have pulmonary tuberculosis of sufficient chronicity and degree to cause indicative physical signs, sputum positive for tuberculosis and manifestations on a roentgenogram of the chest.

With regard to typhoid fever, one may say that the course of illness in this case was not typical of the average case of typhoid. However, in these days when typhoid is a sporadic disease, one sees more atypical than characteristic courses. The description of watery green-yellow stools rouses memories of "pea-soup" and the leukocyte count of 4,500 with 34 per cent neutrophiles fits no other disease quite so aptly. From there on, however, the result of every laboratory test is lined up against the possibility of typhoid. Cultures of the blood and of the stool were negative; one set of agglutination tests suggests agglutination in a dilution of 1:80—which is certainly doubtful in any case—but similar tests done both before and after this one are entirely negative. These are procedures which are performed commonly and which should have been positive sooner or later if the patient had typhoid.

Coming back to amebiasis: The only way to be positive of the diagnosis of this disease is to demonstrate the causative parasite in the feces or in the tissues. Stool examinations were negative in this case, but the demonstration of amebae is notoriously unsuccessful. Amebiasis would explain, better than typhoid fever, the pulmonary symptoms (of which the patient apparently complained more than the intestinal) which one could account for on the basis of multiple abscesses too small to be demonstrated in a roentgenogram. In this case ulcerative lesions in the intestine, with perforation of one of the ulcers, might be suspected.

Clinical Diagnosis: Amebiasis with perforation of intestinal ulcer.

DISCUSSION BY PATHOLOGIST

DR. W. W. MCLAUGHLIN*: The peritoneal cavity contained about 400 cc. of turbid yellow fluid and the peritoneal surfaces were covered with much patchy friable exudate. In the mid-portion of the transverse colon there was a 4 mm. perforation which was partly covered by adherent fatty tissue. This perforation was in the base of an ulcer which was deeply undermined. There were numerous ragged, "moth-eaten," often undermined ulcers measuring up to 2 cm. across in the colon which were characteristic of those produced by amebiasis. They were more numerous in the proximal portion of the colon; the sigmoid was not involved. Histologically, some of the ulcers had a typical flask shape and amebae were present.

The right lung weighed 650 grams. The lower lobe, hyperemic and edematous, contained patches of consolidation plus several ragged cavities.

There was fibrinous exudate over the pleural surface. The bronchi were hyperemic. Histologically, the pneumonia was found to be secondary to aspiration, with formation of multiple abscesses. This may well have been associated with the peritonitis, which may have preceded the pneumonia. The abscesses in the lung did not resemble amebic abscesses and did not contain amebae. Some of the changes in the right lung were old enough to have accounted for the respiratory symptoms noted clinically in late December. However, separate unrelated pneumonia at this time is another possibility. An incidental finding was healed cirrhosis of the liver.

*Fellow in Pathology, Service of Stanford School of Medicine.

California Cancer Commission Studies*

Chapter XVIII

Cancer of the Breast

ALSON R. KILGORE, M.D., *San Francisco*

EARLY breast cancer and late breast cancer are almost two different diseases. These differences are evident in the clinical picture, the plan of treatment, and the prognosis.

EARLY BREAST CANCER

1. SYMPTOMS. *There are none.* In all but a few cases, attention is first called to the breast by the *accidental* discovery of a lump which had previously given rise to no sensation whatever. In only about 1 per cent does pain or discomfort come first. So uniformly true is this that a woman who *finds a lump because of pain or tenderness* can almost be assured that she does not have cancer. Rarely, eczema of the areola or bloody discharge from the nipple are the first symptoms of cancer.

It is time to change emphasis in lay education. A quarter century of persistent publicity has taught women to seek medical advice promptly on the discovery of a lump in the breast. They now go to a physician within a week or two instead of waiting a year or more. Consequently the percentage of cases operated upon before axillary metastasis occurs has doubled or more than doubled. But it is unbelievable how large lumps can become before *accidental discovery.* All too frequently cancers have time to grow to walnut size or even larger before they are found.

Nor is the annual "check-up" a trustworthy assurance of early discovery. A cancer beginning just after one examination may well become incurable before the next year's visit to a doctor. We should teach women to feel their own breasts. Lying in bed or in the bath (not sitting, with the pendulous breast doubled over by its own weight) a woman ordinarily can feel the usual hard lump of cancer when it is no larger than a pea.

2. SIGNS. There are none, except the presence of a lump. The secondary signs of skin or nipple retraction are produced by the contraction of new connective tissue developing with the tumor, and this requires time. The very presence of these changes is proof that the cancer is no longer early. Pig-skin changes, ulceration, fixation to the chest wall, secondary skin nodules indicate even later disease. Palpable axillary nodes (unless large and hard or fixed) may be only inflammatory and so are unreliable as a sign of cancer. *In the earliest cases, when the prospect of cure is brightest there are no signs by which the lump of cancer can be distinguished with certainty from a benign lump.*



Figure 1.—Skin retraction produced by "traumatic fat necrosis"—indistinguishable from that of cancer. (Traumatic Fat Necrosis of the Female Breast and its Differentiation from Carcinoma. Lee, B. J., and Adair, F. E., Ann. Surg., 80: 1924: 670-690).

It is perhaps worth noting that even the late sign of skin retraction is not always pathognomonic of cancer. It has been observed over cysts in which there has been infection. And about half of the cases of innocent lipogranulomatosis (traumatic fat necrosis) will present skin retraction indistinguishable from that caused by cancer. (Figure 1.)

First, it is essential to determine that there is a lump. Areas of thickened breast commonly confuse patients and frequently confuse doctors. About half of the "lumps" that cause patients to seek medical advice prove to be such areas of thickened breast and not true lumps. In addition to examination sitting or standing, if the patient reclines with hands over head, and the breast is examined with the flat of the hand and not between thumb and fingers, such areas of thickened breast will usually "scatter" and lose their definition. It is worth while acquiring experience in order to make the distinction with assurance.

After it is determined that a true lump is present, no amount of further clinical examination will determine its nature. A clump of cysts can be as hard and as irregular in contour as any cancer. Cancer can even mimic the feel of an encapsulated adenoma or of a tense cyst. There is only one safe rule—*every single lump in the breast* must have its nature proved.

3. PROGNOSIS. Nothing so emphasizes the difference between early and late breast cancer as a comparison of "cure rates" based on amount of spread

*Organized by the Editorial Committee of the California Cancer Commission.

outside the breast which time has permitted. On average, these are about as follows:

Axillary Nodes Involved (pathologically proved)	Per cent of patients clinically well at five years
None	70
One	20-40
Multiple	5-10

4. Exploration. Delay between exploration and radical operation for cancer of the breast substantially reduces chances of cure. This principle should by now be settled and universally accepted. *No physician should ever explore a lump unless he is prepared and able to do an immediate radical operation.* It is necessary that diagnosis be completed at the time of exploration. Frozen section facilities and competent pathological judgment should be available whenever any lump in the breast is surgically exposed.

Since even frozen section diagnosis is not always entirely conclusive and does consume at least some time with the patient waiting on the operating table, the surgeon who undertakes exploration of breast lumps can and should acquire sufficient experience to recognize the gross characteristics of the common lumps encountered:

(1) *The encapsulated* lump which can be shelled out with blunt dissection is usually one of the benign adenomas. It may be a lipoma, a dermoid cyst or other non-indigenous tumor. But, while cancers occasionally present a sharply defined margin without grossly visible infiltration, they are not truly encapsulated.

(2) *Cancer* is densely hard, cutting like sanded cartilage, with surface grayish (rather than the pure glistening white of normal breast), with dirty yellow or grey white streaks instead of healthy yellow fat, and fixed to if not actually infiltrating surrounding tissue. When sectioned the cut surface retracts, instead of bulging as does the adenoma.

All usual histological types of cancer present the same gross characteristics, except duct carcinoma spreading along duct spaces rather than forming a defined mass, and colloid or gelatinous carcinoma. A cancer 5 mm. in diameter has the same gross characteristics as one of walnut size.

(3) *Normal breast tissue.* The breast is composed of (a) gland structures—ducts and lobules—carried in (b) connective tissue stroma, padded with (c) fat. Gland structures in the inactive or atrophic breast are too small for naked eye recognition. But if ducts are dilated or lobules hyperplastic they may be recognized—the latter as grayish or flesh-colored, pinpoint to pin-head structures often very slightly elevated in freshly cut tissue. Breast stroma is a glistening white connective tissue, extremely flexible and compressible (so much so that it is almost impossible to cut blocks for sections until fixed).

The relative amounts of stroma and fat vary greatly from center to periphery of the same breast, with age and habitus of the individual, with phase of menstrual cycle, etc. But the stroma and fat elements are recognizable in non-tumorous breast tissue and hyperplastic lobules or dilated ducts.

(4) *Cystic disease.* (a) *The simple cyst* with "blue dome" before opening, with cloudy but non-bloody fluid, with smooth wall and normal breast tissue around it is often single but frequently multiple.

(b) *Hyperplastic or papillary cystic disease* presents a confusing variety of pathological pictures. There may be a single cyst or clump of cysts containing papillomata, or an entire breast may be filled with larger and smaller cysts. Areas may show hyperplastic ducts plugged with their overgrown epithelium so as to leave almost no recognizable normal breast tissue. It is this form of cystic disease, fortunately uncommon, which presents greatest difficulty in gross diagnosis. But it presents difficulty in frozen section diagnosis as well (and sometimes even in diagnosis with the best of paraffine sections). When it occupies a large part or all of a breast, it is the one condition for which a radical operation must occasionally be done without certainty that cancer actually exists.

When it comprises only a local area, however, it can usually be distinguished from cancer. And in the single papillary cyst, examination of the base of the papilloma will disclose presence or absence of the previously mentioned characteristic features of carcinoma.

Frozen section diagnosis is not always finally correct. Sections are seldom as well fixed, cut and stained as by good paraffine technique and it is possible to miss the "business part" of a specimen in hurried frozen section examination. The gross appearance is frequently sufficient and may occasionally be more reliable than frozen section. It should be studied at every breast exploration.

THE OPERATION FOR CANCER

The standard radical operation is based upon (1) the lymphatic anatomy (Figure 2)—drainage to the deep fascia, both directly and by a surface plexus communicating with the deep fascia lymphatics over the margin of the breast, or drainage to the axillary lymphatics both around and *through* the pectorals and (2) the tendency of breast cancer to spread by solid growth along lymph-channels. The purpose of the operation is to remove as much tissue into which cancer may have spread as may be done without an operative mortality (or morbidity) out of proportion to "cure rate." It consists in removal of the breast and its overlying skin, of the deep fascia from mid-line to posterior axillary line and from sternoclavicular joint to upper abdominal rectus, both pectorals (except the clavicular bundle of the major) and the lymphatics about the axillary vein (with the fat in which they lie). All this tissue is removed *in one mass* to avoid opening cords of cancer which may be growing in lymph channels. (Figure 3.)

This should be the minimum operation for any cancer, however small. Size of primary tumor is no indication of extent of spread. Still more extensive procedures—resection of clavicle and neck dissection, even shoulder girdle amputation—have been proposed for selected cases. But general opinion is

that the questionably increased "cure rate" resulting is insufficient to justify the increased mortality and morbidity.

Whether the operation is done with cold knife, cautery or electric current dissection is a matter of the surgeon's choice. The extent of actual cauterization is small and if cutting is done so close to cancer it might as well not be done. Usefulness of cautery or electric cutting is in reducing blood loss and operating time.

RADIATION SUPPLEMENTING SURGERY

There appears to be generally growing conviction that routine irradiation before or after operation adds little if anything to percentage of "cures." A course of irradiation planned to sterilize cancers is a very major procedure. Many patients subjected to it have volunteered that they would prefer suicide to a second similar experience. Nor is such treatment without risk of substantial and lasting ill effects—pulmonary fibrosis, cartilage necrosis, brachial neuritis, peri-articular fibrosis with stiffening of the shoulder. Without substantial gain in "cure rate" over operation alone, routine pre-operative or post-operative irradiation seems unjustified.

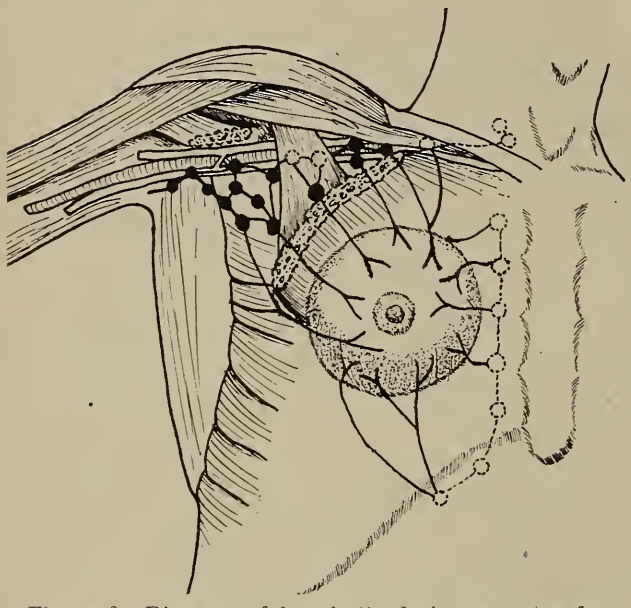


Figure 2.—Diagram of lymphatic drainage routes from breast—(1) to axilla *through* as well as around *both sides* of the pectorals (and "Wainright's gland" between the two muscles)—(2) via deep fascia to the intrathoracic internal mammary chain—(3) to abdomen via rectus fascia.

CYSTIC DISEASE AND CANCER

Unless one regards a normal breast as a "precancerous condition" and removes all whose owners will hold still (at, say, 45) he should not delude himself and be dishonest with his patients by advising mastectomy because of the presence of abnormalities which are no more likely to produce cancer than is normal breast.

Such is the "blue-domed" cyst, single or multiple. Once its nature is established, it (and all its associated smaller cysts) may be let alone so far as safety is concerned.

The much less common (1:10) form of cystic disease characterized by extensive papillary and solid epithelial overgrowth has been the subject of more debate than any other breast disorder. Opinion has varied from regarding it as equally as harmless as simple cysts to the belief that it frequently produces cancer. This author's opinion is that the true facts lie between the extremes—that grossly demonstrable hyperplastic cystic disease is somewhat more prone to malignant degeneration than is normal breast. Therefore, he believes that so much of breast tissue as shows this form of cystic disease in its gross characteristics should be removed for protection—whether removal involves an intraductal papilloma, a single papillary cyst or clump of cysts, a localized area of diffuse change or even the entire breast if extensively involved.

NIPPLE DISCHARGES AND EROSIONS

Non-lactating duct mouths are normally closed with a plug of desquamated epithelium. If such a plug be dislodged, fluid present in ducts appears as a discharge and is without significance. It may vary from watery or creamy to green or brown and may come from several ducts.

If the discharge contains blood, however, it invariably indicates intraductal disease of some kind. Gross appearance of the fluid cannot be trusted to determine presence or absence of blood. Dark brown fluid, leaving stains on clothing like dried blood, may be innocent. Clear watery fluid may contain red blood cells. *Microscopic examination is required of all nipple discharges.*

In perhaps 90 per cent of cases of bleeding from the nipple, the source is one or more benign intraductal papillomata, while in the rest it comes from carcinoma. The ratio of cancers to papillomata increases, however, with advancing age. Some authorities have estimated that, in women over 50, bleeding comes from cancer in nearly 50 per cent. The source of bleeding must, therefore, be determined and appropriately dealt with.

Bleeding papillomata may be located anywhere in the breast but are most common in the larger ducts beneath or at the edge of the areola.

If a lump is palpable, it is explored and dealt with in accordance with its character.

More commonly, no lump can be felt, since the papilloma is too soft.

Transillumination may, by a dark shadow, show the location of a pool of blood about a papilloma. In this author's experience, it has been of infrequent help.

The location of the discharging duct mouth over the nipple may suggest the quadrant in which the papilloma lies.

Gentle pressure with finger-tip on successive points about the areola may indicate the source as discharge appears at the nipple. Other more precise methods failing, excision of a zone of breast about such a point has occasionally been successful.

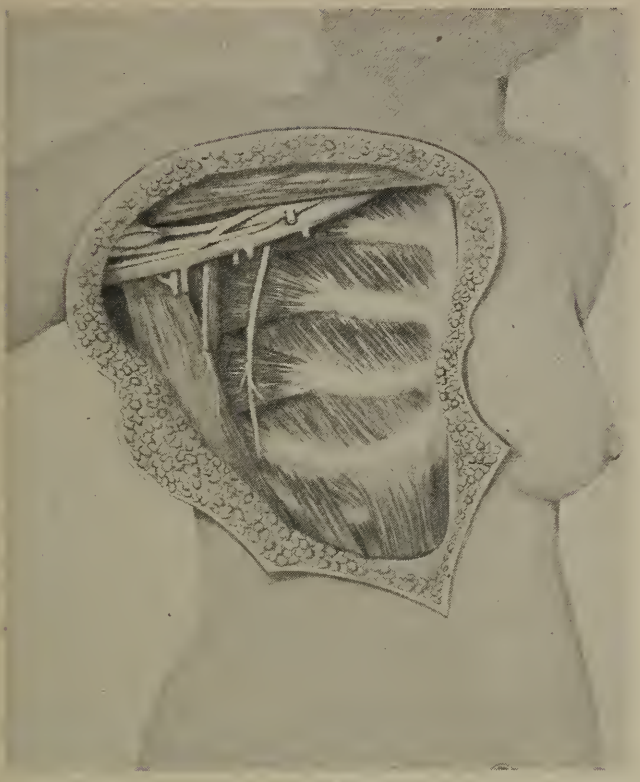


Figure 3.—Extent of removal of tissue by radical mastectomy. (From Lewis' Practice of Surgery, W. F. Prior Co., Vol. V, Chapter 6).

A very useful procedure is to milk a tiny drop of discharge to identify the duct, introduce the eye end of a small cambric needle as a probe, and split the duct on the needle as a guide until one or more papillomata are exposed.

Rarely the source cannot be located. A safe course to follow would be as follows: if the patient is a young woman, repeated observation will eventually reveal the source. If the patient is elderly, a simple mastectomy with immediate careful examination of the entire breast is indicated, since about half may show cancer.

Erosion or eczematoid conditions of the nipple, however small, which *do not yield promptly to conservative treatment,* virtually always come from intraductal disease, either cancer or precancerous hyperplasia. They require at least simple mastectomy—radical operation if cancer be found. The association of duct cancer with Paget's disease of the nipple, even in the absence of palpable underlying disease, is so constant, that *the diagnosis of Paget's disease demands radical mastectomy.*

LATE CANCER

Skin or nipple retraction, direct skin involvement or ulceration, "pig-skin," secondary skin nodules, large and hard axillary nodes and demonstrable distant metastases are clear evidence that the cancer is no longer "early." The problem is no longer one of diagnosis but of whether the disease is beyond even a small chance of cure by surgical operation. To subject a certainly incurable patient to radical operation does not prolong life, offers little or nothing of palliation and reflects discredit on operation for breast cancer. And, although perhaps not subject to statistical proof, clinical impression suggests that patients with incurable cancer do less well following radiation therapy if they have been operated upon.

It is this author's conviction that *surgically incurable cancer cannot be made surgically curable by irradiation,* however much the clinical appearance may be changed. If it is incurable in the first place, this is because cancer has spread beyond the field of radical operation. If cancer could be sterilized outside this field, it could be sterilized within it and there would be no reason for operation. If it cannot be sterilized outside the field of operation, operation will not cure it.

On the other hand, much relief (even an occasional "cure") can be offered by irradiation for inoperable cancer.

Each cancer of the breast should be surveyed in the first instance for surgical curability. Operations should be done for early cancer and even more advanced cancers not demonstably incurable. Surgically incurable cases should be selected for irradiation and *this method of treatment adhered to* throughout management. The only possibly useful surgical treatment is an occasional simple mastectomy to remove a primary mass too bulky for irradiation or to prevent or relieve ulceration of tumors proved insensitive to irradiation.

What signs are factors in the determination of curability?

Surgical cure may still be possible in the presence of the following signs:

1. Skin or nipple retraction.
2. Local skin involvement and ulceration. Some cancers—colloid for example—may reach large size and ulcerate before metastasizing.
3. Small movable axillary nodes.

Diagnosis of axillary metastasis by palpation is notoriously inaccurate. About a third of palpable nodes prove innocent; and in about the same proportion of cases, metastases are found pathologically even though no node was felt before operation.

Surgical cure is considered impossible and the patient should not be operated upon when the following signs are present:

1. Large, hard, fixed, axillary nodes. In these cases metastasis is a certainty. When metastasis has extended in a chain of nodes to the upper limit of an operative field, the probability of metastasis beyond the limits of surgical operation in the same or in other directions is overwhelming. In the author's experience, the presence of one hard fixed node, 2 cm. or more in size, indicates multiple node involvement and it is his conviction that such cases are surgically incurable.
2. Supraclavicular metastasis.
3. Pig-skin changes, extensive skin edema and secondary skin nodules. These are clear evidence of extensive involvement of lymphatics.

4. Distant metastasis. It is advised that chest and bone roentgenograms be made, the latter to include skull, spine, pelvis, humeri and femora. Evidence of metastasis, of course, precludes radical mastectomy.

5. Inflammatory cancer, a very rapidly growing, highly malignant cancer, usually in younger women. The whole breast is "frozen" early in the disease, the skin red, edematous and hot. It is uniformly fatal. Operation is useless. Even the needle punctures of ill-advised attempts to aspirate may start ulceration.

SIMPLE MASTECTOMY FOR CANCER

In feeble, aged women mastectomy to remove cancer from attention and worry may occasionally be justified. Very rarely it may be desirable to relieve an incurable patient of an ulcerating mass *proved radioresistant. In the usual treatment of breast cancer, simple mastectomy has no place.* Very early metastasis cannot be demonstrated clinically. With very early metastasis there is still a chance of cure by radical operation and no chance if the metastases are left.

Simple mastectomy plus irradiation as a standard treatment is without logic. If radiation could be depended upon to sterilize cancer outside the breast, it could sterilize it even more readily within the breast and no surgical operation would be necessary.

HORMONE THERAPY

There is as yet no general opinion and accepted practice concerning the use of hormone therapy in the treatment of breast cancer.

Surgical castration or ovarian irradiation has been followed by relief of pain from, and recalcification of, bone metastases. Adair has stated that improvement occurs in about 13 per cent of cases but that prophylactic ovarian irradiation does not reduce incidence of bone metastases. It does not cure the disease and does frequently add sudden severe menopause symptoms to a younger woman's discomfort.

Testosterone has been reported upon by a number of authors with varying conclusions. Adair finds that, given in large doses, it has favorable effect on bone metastases—both pain relief and recalcification. He suggests 100 mg. testosterone propionate intramuscularly three times a week for ten weeks followed by 40 to 60 mg. methyl testosterone by mouth daily for eight weeks. In such amounts it is likely to produce masculinizing effects and is certainly expensive. It would seem perhaps that the chief usefulness of both ovarian irradiation and testosterone will be found in the presence of bone metastases insensitive to direct irradiation or when no more irradiation can safely be given.

More recently, a number of reports indicate that stilbestrol in women well past the menopause may yield remarkable regression, especially of soft tissue lesions. No standard dosage can yet be laid down. Recommendations vary from 1 to 2 mg. up to 15 mg. daily. Even larger doses have been given without apparent ill effect (except recurrence of uterine bleeding, subsiding after withdrawal).

SUMMARY

1. Most breast cancers are discovered accidentally as painless lumps. They should be found earlier by intentional search.

2. Clinical examination should determine the presence or absence of a true lump. It cannot safely distinguish between benign and malignant lumps.

3. At exploration, frozen section facilities should be available and immediate radical operation done for cancer.

4. Blood-containing discharge from the nipple indicates either cancer or a precancerous lesion. Its sources must be established and dealt with.

Cancer of the Bladder, by A. J. Scholl, M.D., and Cancer of the Prostate by R. A: Barnes, M.D., Chapters XXIV and XXV of the California Cancer Commission Studies, will be published in this section in the December issue of CALIFORNIA MEDICINE.

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EDITORIAL

Banking on Blood

The value of blood as a therapeutic agent is so universally recognized today that scientific argument on it has ceased. On the other hand, the means and methods of obtaining and distributing human blood and blood derivatives continue to form the basis for much argument that is not all scientific.

Present-day discussion along these lines extends from coast to coast and border to border. A variety of opinions emerges, each type attracting its own adherents, but the basic question appears now to come down to about this: Should blood be distributed gratis by publicly-supported social agencies or should it come from self-supporting non-profit organizations which contribute scientific control and are largely in the hands of the medical profession? This question has been highlighted in the past year by the entry of the American Red Cross upon the blood banking scene. The Red Cross has adopted a national policy of fostering blood banks in all major cities of the country for the collection and distribution of blood, without charge, to all who may need it.

The possibility of disrupting established community non-profit blood banks has been seen by the Council of the C.M.A. in the Red Cross program. It has been discussed in the A.M.A. House of Delegates. The discussions resulted, early this year, in the appointment by the C.M.A. Council of a Blood Bank Commission, composed of members known for their interest in and knowledge of modern blood banking methods. This commission has actively worked toward the establishment of blood banks at the community level in strategic California cities and has achieved a large measure of success in its first few months of operation. The commission has discovered throughout the state a lack of knowledge of the underlying considerations of the Red Cross program as compared with the non-profit approach which has been so successful in this state.

Because the following progress report made by Dr. John R. Upton, chairman of the Blood Bank Commission, raises questions that will arise in your own community one of these days, if they have not already done so, it is highly recommended reading.

* * *

"A long range blood bank program has been planned for the State of California. If it is to be carried through, a full understanding of the present blood bank system is necessary. To this end, the following summary of pertinent facts:

"At present there are blood banks of five different types operating in the state. There are seven community or non-profit banks, eight county hospital banks, sixteen banks in private hospitals, several privately owned banks run for profit, and at least four in which the Red Cross is interested and from which blood is dispensed free of charge.

"In 1946 the California State Department of Public Health appointed a committee to study the blood coverage requirements of the State, to suggest a plan of action, and then to write a bill for presentation to the State Legislature. Representatives of the California Medical Association, county medical societies, community blood banks, osteopathic surgeons, Hospital Conferences, and California State Nurses' Association were interviewed. An excellent survey of the state was made by the Department of Public Health. Out of the long and exhaustive meetings

came Senate Bill Number 1257. This bill was presented to the Legislature in January of 1947 and was defeated. By its defeat, the State Blood Bank Program was set back at least three years.

"Basic principles of the bill were: The Department of Public Health would sponsor and aid in the establishment of community blood banks in areas which required the service. Operation and control of the banks were to be vested in the local county medical society. A maintenance, or service charge, was to be made for blood, and the blood would be replaced by a relative or friend of the person receiving it. Operating standards were to be set and maintained by the State Department of Public Health in accordance with regulations set forth in the Biologics Act.

"If the bill had become law, a tremendous stimulus would have been given local medical societies to establish community blood banks. When the bill was defeated, the Red Cross, cognizant of the dramatic aspects of blood banking, quickly entered the picture. The aim of the American Red Cross was to provide 'free blood for all.' This, their early slogan, was a most cruel misrepresentation of fact, for the plan called for the expenditure of 20 million dollars a year. You and I are the Red Cross. We have maintained (Editorial, CALIFORNIA MEDICINE, November, 1947) that a medical program such as blood banking is beyond the proper scope of the Red Cross. We stoutly believe that the recipient of blood should pay the small processing charge and provide a donor to replace the unit of blood which he received. The Bank should be self-supporting; it should be a community bank. Because years of experience have taught us the difficulty of getting even relatives and friends of the recipient to donate their blood, we cannot see how the Red Cross can indefinitely expect large numbers of people to donate for total strangers. A modern blood bank program is a far cry from the Red Cross blood procurement set-up of war days. The Red Cross centers then just drew blood from donors. The laboratory work, such as typing, Rh studies, and serology, was all done by commercial laboratories. The Red Cross Blood Program was a project well performed, but to try to change a war measure into a peace-time function and to expand that service into a full scale medical program is not within the province of the Red Cross.

"For the sake of the record, we emphatically state that our one main point of controversy with the American Red Cross is its demand that the patient shall not be required to pay a service charge for the blood received or to assume any moral responsibility for replacing the blood used. It goes without saying that no one has been or will be deprived of blood because of real inability to pay a service charge or to provide replacement. But aside from that, who *should* pay for the bottle in which the blood is stored, the rubber tubing, the needle, and the tests of serology, typing and Rh factors, and the salaries of technical personnel—for all the varied and intricate steps and checks that make for 'guaranteed blood?' Shall the recipient pay the modest non-profit service charge or shall strangers be asked to carry this financial load by their annual donations to the Red Cross?

"Efforts to get the American Red Cross to compromise this basic issue of the service charge and donor replacement have been to no avail, although many local Red Cross chapters are in full accord with our principles and would be happy to work harmoniously with the local county medical societies and their community blood banks. This willingness has been thwarted by the National Chapter, and to make matters worse the local chapters of the Red Cross were forbidden to aid in the 'permissive' program. We would welcome the participation of the Red Cross in the blood bank field if it would modify the socialistic features of its program. We would welcome its assistance in procuring donors, staffing canteens, and distributing blood on call to hospitals. The Red Cross can have the publicity; Medicine wants to give service. Our state-wide plan could well use the facilities of the local Red Cross chapters; they, in turn, would once more receive the necessary moral and ethical support of the medical profession. Each agency requires the enlightened and enthusiastic support of the other. The original premise of the Red Cross is to bring succor to the needy in time of emergency or disaster; that same, but greatly expanded, humanitarian principle has been espoused by the medical profession since its earliest beginning.

"When Senate Bill 1257 was defeated by short-sighted interests, the California Medical Association Council felt morally obligated to help. Its only interest in the Blood Bank Program is to see that people of the state are provided with adequate blood coverage. The plan of action is identical to that outlined in the defeated Public Health Bill. We stress the same fundamental points: the Public Health Department will maintain standards; the local county medical societies will operate and control the blood banks, and these banks will be supported by those who use the transfusion service.

"There are approximately 36,000 hospital beds in California. It is well established in medical statistics that approximately 180,000 units of whole blood per year is needed to serve that number of beds. (Five units of blood per bed per year is the amount required when adequate facilities are available and when the entire medical profession is fully cognizant of the therapeutic value of blood and its various derivatives.) Forty-six of the state's fifty-eight counties have little or no access to blood for transfusions. This woeful discrepancy must and will be corrected. Regional community blood banks are badly needed right now throughout heavily populated areas such as Los Angeles, Fresno, Bakersfield, and Santa Barbara. Just to mention a few potential sites, smaller banks might well be supported in Redding or Chico, Visalia and Ventura. Sacramento opened its community bank in October; members of the Sonoma County Medical Society assessed them-

selves in order to underwrite a similar bank in Santa Rosa.

"Many people still think that blood banks are needed only during a war, that only war's wounds require blood transfusions. That thought is entirely erroneous. Democracy's battlefields have, in the past, been her highways, her farms, and her great industrial plants.

"What of the future? What of the medical problem posed by just two recent developments, supersonic speed and the atomic bomb? Blood and blood plasma will form the therapeutic keystone in the treatment of casualties when and if a Hiroshima occurs in this part of the country. Adequate blood coverage for the state, high standards of service, coordination of all banks, reciprocity between banks, similarity of blood banking procedures, fast and efficient distribution systems, adequate mobile units geared to serve inaccessible areas, auxiliary substations, walking blood banks—these and many other problems present themselves for speedy and precise settlement. These are medical problems of the medical profession.

"We must gird for the long tasks and work together for the common weal. Let's get on with the job. Tomorrow may be too late. The solution rests with organized medicine. Why should not California have its own state-wide blood bank program, sponsored, implemented and operated by physicians?

"John R. Upton, M.D.,
"Chairman, C.M.A. Blood Bank Commission."

Letters to the Editor . . .

Tuberculous Lympholysis

It was shown by Rich,[5] Heilman[3] and others that splenic explants from tuberculous animals are killed when grown in concentrations of tuberculin that are harmless to normal tissue explants. Meyer[4] found that this hypersusceptibility is not a manifestation of classical anaphylaxis, since explants from animals sensitized to horse serum are not injured by the addition of horse serum to the culture fluid.

Detailed study of this cellular hypersensitivity is reported by Favour[1] of the Rockefeller Institute. Tuberculosis was produced in mice and guinea pigs by subcutaneous or intravenous injection of six to ten-day-old cultures of tubercle bacilli. Mice surviving three to four weeks and guinea pigs surviving two to six months were selected for cytologic study.

Suspensions of guinea pig lymphocytes, monocytes and granulocytes were prepared from pooled blood samples by the cell fractionation technique suggested by Ferrebee and Geiman.[2] This fractionation is based on the different specific gravities of different white blood cells, and their centrifugation from suspensions in standard dilutions of bovine albumin. A similar technique was used in fractionating suspensions of mouse splenic cells.

Toxic effects were demonstrated by adding 0.2 cc. cell suspension to 0.2 cc. dilute tuberculin (or other bacterial extract, such as S. enteritidis extract) in 0.5 cc. albumin solution. Lytic effects were measured by the resulting reduction in differential white cell count at the end of 60 to 90 minutes. In a typical experiment a suspension of splenic cells from a tuberculous mouse was reduced from an initial white cell count of 15,890 to 12,680 by 60 minutes' exposure to dilute tuberculin. Differential counts showed that this reduction was due to a 56 per cent reduction in lymphocytes unaccompanied by a loss of other cell types.

In a second experiment there was by the end of 90 minutes a 36 per cent lysis of lymphocytes from a tuberculous guinea pig, with no distinction of other cell types. Lymphocytes from normal mice or guinea pigs or from animals infected with S. enteritidis were not lysed by the same concentration of tuberculin. Lymphocytes from animals infected with S. enteritidis, however, were specifically lysed by soluble substances derived from cultures of S. enteritidis. Control tests with lymphocytes from normal or tubercular animals were not lysed by any extract thus far tested. Tubercular lympholysis can also be demonstrated in fresh heparized mouse or guinea pig blood to which tuberculin is added.

No theory is as yet proposed to explain this acquired specific lymphocyte hypersensitivity. Conceivably it is due to a specific activation of autolytic enzymes, a futuristic theory of possible clinical interest.

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Stanford University
Palo Alto

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NOTICES AND REPORTS

Executive Committee Minutes

Tentative Drafts: Minutes of the 210th, 211th and 212th Meetings of the Executive Committee of the California Medical Association.

The meeting was called to order by the Chairman at the Family Club, San Francisco at 7 p.m., Wednesday, July 21, 1948.

Roll Call:

Present were President Askey, President-Elect Kneeshaw, Speaker Alesen, Council Chairman Bruck and Auditing Committee Chairman Shipman, Chairman of the Executive Committee. A full committee present and acting. Ex-officio member present: Secretary-Treasurer Garland. Ex-officio member absent, Editor Wilbur.

Present by invitation were Doctor Dwight H. Murray, Chairman of Committee on Public Policy and Legislation; Doctor C. K. Cooley, secretary of California Physicians' Service; Mr. Ben H. Read, executive secretary of the Public Health League of California; Mr. Clem Whitaker, Public Relations Counsel; Mr. Howard Hassard, Legal Counsel, and Mr. John Hunton, Executive Secretary.

1. *Selective Service:*

A letter from Governor Earl Warren of California was read, in which he requested that physicians in various areas of the state be selected for appointment to medical advisory boards under the new Selective Service Act. The appointees would be called upon to review cases where manifestly disqualifying conditions were claimed by potential draftees, the armed services performing their own induction physical examinations. On motion duly made and seconded, it was voted that the county medical societies in the areas involved be asked to nominate physicians for such appointment.

2. *C.M.A. Constitution and By-Laws:*

It was pointed out that the 1948 House of Delegates had approved a resolution calling for the appointment of a five-member committee to review the Association's Constitution and By-Laws. On motion duly made and seconded, it was voted to refer this matter to the Chairman of the Council, which body should consider the Chairman's recommendations for such appointments at its next meeting.

3. *State Department of Public Health:*

Doctor Bruck reported that he, acting as a member of the committee to study chronic diseases for the State Department of Public Health, had declined to send to the secretaries of the county medical societies a letter which he believed to contain leading questions. Instead, a modified version of this letter, prepared by a representative of the State Department of Public Health, had been sent; however, the original letter had been sent to county health officers by a county health officer who is also a member of this study committee. It was agreed that copies of both letters should be sent to all members of the Council so that they could see the approach being made on this question. (Copies of both letters are attached hereto and made a part of these minutes.)

The recent action of the American Public Health Association in appointing a committee for the creation of a section on medical care was discussed and it was regularly moved, seconded and voted that the American Medical Association be requested to secure adequate representation at meetings of the American Public Health Association.

4. *California Society for Crippled Children-Epilepsy Program:*

Doctor Bruck reported that further conferences had been held with representatives of the California Society for Crippled Children and that a definite program appeared in the making, with the proposed case-finding program to be abandoned and with the county medical societies to handle the program in their own areas. A further report is to be made to the Council.

5. *Public Policy and Legislation:*

Doctor Murray reviewed some of the measures which will appear on the November general election ballot as initiative measures and placed particular

emphasis on the so-called "Bill of Rights" or "Omnibus" proposition, No. 11. He pointed out that this bill would create a board of naturopathic examiners which would thereafter control the licensing of all practitioners in all the healing arts. It was brought out that a taxpayer's suit has been filed against the Secretary of State to prevent this measure's appearing on the ballot and that the C.M.A. had been asked to appear as a friend of the court in the matter. After discussion it was regularly moved, seconded and voted that legal counsel be authorized to appear on behalf of the Association in this case.

6. *California State Chamber of Commerce:*

A request from the California State Chamber of Commerce to contribute $1,000 to the Chamber's work was read and it was regularly moved, seconded and voted that the Association make such a contribution this year.

7. *California Physicians' Service:*

Doctor C. L. Cooley, secretary of California Physicians' Service, reported that C.P.S. is now operating in the black and the present reserve in the unit stabilization fund is about $360,000. He also reported that C.P.S. is dealing with the Veterans Administration relative to a new VA regulation which holds that preliminary examinations to determine service-connected disabilities may not be paid for unless prior authorization from the Administration has been received. This regulation would mean that the first call on physicians by eligible veterans would not be paid for, and C.P.S. is endeavoring to secure its repeal. He also stated that the C.P.S. board of trustees has taken over as its own sub-unit the fee schedule committee headed by Doctor William L. Bender and originally appointed by the C.M.A. Council.

8. *Veterans Administration:*

The Secretary reported that the Veterans Administration was considering setting up a diagnostic center in Sacramento and another in Stockton, presumably for all examination of veterans claiming disability ratings but so laid out that full diagnostic and treatment facilities might well be made available. After discussion it was regularly moved, seconded and voted that it be the opinion of the Executive Committee that adequate machinery exists for the examination and rating of veterans claiming disabilities and that the county medical societies be encouraged to oppose the establishment of such local diagnostic centers as superfluous and unnecessary.

9. *Legal Department:*

Mr. Hassard reported that the Association of California Supervisors had met in July and had adopted a resolution calling for the recognition by county boards of supervisors of the shortage of hospital beds and the attempt by such boards to secure state and federal funds in aid of hospital construction. This would mean the competition of county hospitals with non-profit voluntary hospitals and a disadvantage to the latter in attempts to secure public funds for expansion. Mr. Hassard reported on a letter received from a member who has opened a pathological laboratory in association with other physicians who refer their work; the laboratory has been incorporated and the question of the ethics of such a procedure was raised. It was regularly moved, seconded and voted that this matter be referred to the next meeting of the Council and the physician be advised that the entire matter of such ethical considerations was under study; it was agreed to recommend that a full code be prepared on the ethical approach to the rebate question.

10. *Proposed Hospital-Radiologist Contract:*

Mr. Hassard reported that a committee of the Association of California Hospitals had reviewed the recent opinion of the State Attorney General, in which it was held that hospitals employing physicians on a salary basis were violating the corporate practices sections of the medical practice act, had recognized the validity of this opinion and had been instructed by that association to proceed with the drafting of standard types of contracts between hospitals and physicians to cover the rendering of professional services in hospitals. Doctor Garland presented a specimen contract which he proposed be used as a base for the variety of contracts needed in such cases and it was regularly moved, seconded and voted that legal counsel be authorized to discuss with the committee and legal counsel for the Association of California Hospitals the drafting and adoption of standard type or types of contracts to cover the rendering of professional medical services in hospitals.

11. *C.M.A. Employees' Retirement Plan:*

Doctor Alesen reported that the committee to consider a pension retirement plan for Association employees had approved a type of insurance contract offered by the Northwestern Mutual Life Insurance Co. There was discussion as to the number of employees to be covered by such a program and it was agreed that the matter be discussed further at the next meeting of the Council.

Adjournment.

SIDNEY J. SHIPMAN, M.D., *Chairman.*
L. HENRY GARLAND, M.D., *Secretary.*

211th Meeting

The meeting was called to order by Chairman Shipman at 6 p.m., Sunday, August 22, 1948, in Room 210 of the Sir Francis Drake Hotel, San Francisco.

Roll Call:

Present were President Askey, Speaker Alesen, Council Chairman Bruck and Auditing Committee Chairman Shipman, chairman. Absent, President-Elect Kneeshaw. Present by invitation, Legal Counsel Hassard.

A quorum present and acting.

1. *Time and Place of Annual Secretarial Conference:*

After discussion it was regularly moved, seconded and voted that the annual Secretarial Conference be held in San Francisco on February 4 and 5, 1949.

2. *Appointment to C.P.S. Fee Schedule Committee:*

It was regularly moved, seconded and voted that Doctor Herbert J. Kirchner of Los Angeles be appointed a member of the C.P.S. fee schedule committee, to succeed Doctor Harold P. Totten, resigned.

Adjournment.

SIDNEY J. SHIPMAN, M.D., *Chairman.*
L. HENRY GARLAND, M.D., *Secretary.*

212th Meeting

The meeting was called to order by Chairman Shipman at the Family Club, San Francisco, at 5:30 p.m., Wednesday, September 29, 1948.

1. *Roll Call:*

Present were President Askey, President-Elect Kneeshaw, Speaker Alesen, Council Chairman Bruck and Auditing Committee Chairman Shipman, chairman of the committee.

Present, ex-officio, were Secretary-Treasurer Garland and Editor Wilbur.

Present by invitation were Executive Secretary John Hunton; Legal Counsel Howard Hassard; Field Secretary Ed Clancy; executive secretary of the Public Health League of California, Ben H. Read.

Present by invitation during a portion of the meeting were Col. Alvin Gorby, M.C., U.S.A.; Lt. Col. Stuart I. Draper, M.C., U.S.A.; Maj. Donald L. Brubaker, M.C., U.S.A. (U.S.A.F.), and Capt. E. J. Best, M.C., U.S.N.

A quorum present and acting.

2. *Physicians for Military Service:*

Doctor Bruck outlined conferences he had held with Col. Gorby and other officers of the Sixth Army relative to the need of the Army and other forces for medical officers, both present need and anticipated demand under the enlarged forces under the new Selective Service Act. Col. Gorby stated that the present needs of the Sixth Army are for 31 additional medical officers by December 1, 1948, and an additional 60 by January 1, 1949. He stated that the Army tables of organization call for 4.7 physicians per 1,000 active personnel. Capt. Best stated that the Navy now needs 40 additional medical officers in the Twelfth District and 39 in the Eleventh District. Maj. Brubaker stated the Air Force relies on the Army Surgeon General for medical officers but pointed to a need of an unspecified number of medical officers in the near future.

Doctor Bruck reported that the suggestion had been made that the Association work with the armed forces in a campaign to cover the medical schools and teaching hospitals of the state in an effort to recruit young physicians for the military forces. There are now about 4,000 physicians or medical students in the U.S. who have received all or a part of their medical education at federal expense; of this number, only 216 are within the age limits of the Selective Service Act. After discussion, it was regularly moved, seconded and voted that the Association cooperate with all branches of the armed forces in a recruiting program for medical officers throughout the state, the Chairman of the Council to be authorized to activate this program.

3. *Memorial for Philip K. Gilman, M.D.:*

Discussion was held on the establishment of a memorial fund in the Stanford University Medical School in honor of the late Philip K. Gilman, M.D. It was regularly moved, seconded and voted that Doctor Wilbur ascertain from the school the manner in which such a fund might be established and report to the next Council meeting.

4. *State Department of Public Health:*

Doctor Shipman reported on a request received from the State Department of Public Health for assistance in a study to be conducted on methods of control for tuberculosis. Doctor Shipman suggested to the department that a representative of the Association be named on the study committee and the department has requested that such a representative be named. It was regularly moved, seconded and voted that Doctor H. Gordon MacLean be named as the Council representative on this committee.

5. *Public Policy and Legislation:*

An appeal for Association support of Proposition No. 5 on the November ballot was presented. This proposition would increase the salaries of members of the State Legislature from $100 to $250 per month. As an aid in attracting qualified men to serve as members of the Legislature, it was regularly moved, seconded and unanimously voted that the Executive Committee go on record as approving this ballot proposition and that the appropriate members of the Legislature be so notified.

6. *Santa Fe Hospital Association:*

In response to questions, Mr. Hassard reported on the present status of the controversy between members of the staff of Santa Fe Hospital Association, Los Angeles, and the trustees of the hospital. No further action has taken place since the Railway Mediation Board in Chicago declined to intervene in behalf of some physicians who had been dismissed or whose activities had been curtailed by the hospital trustees. It was pointed out that the Board of Medical Examiners, acting under a recent ruling of the State Attorney General relative to corporate practice of medicine, might take steps which could clarify this situation.

7. *Chronic Disease Study—Cancer Commission:*

Doctor Bruck reported that the chronic disease studies of the State Department of Public Health

have progressed to the point where proposed reports on the various sections of the study are under preparation. Members of the C.M.A. Cancer Commission are cooperating in the preparation of the cancer section of the report and Doctor Bruck has been named a member of a committee to edit all proposed sections of the entire report prior to presentation of the report to the entire committee for approval for presentation to the Legislature. If advisable, minority reports may be prepared.

8. *California Physicians' Service:*

Mr. Hassard and Doctor Cooley discussed the proposed plan of the Blue Cross and Blue Shield plans to cooperate in formation of a national organization to underwrite, through local plans, a nationwide coverage of prepayment medical care and hospitalization service. Physicians in some states are opposing this proposal and Mr. Hassard was authorized to meet with these physicians in Chicago on September 30, 1948, in order to advise them that the Executive Committee of the Association has reviewed the proposals and believes them to be sound and workable in principle.

9. *American Medical Association—General Practitioner Award:*

A communication from the A.M.A. outlining the methods to be used in selecting the physician to be honored by award of a token as the outstanding general practitioner of the year, was read and it was agreed that the county medical societies be notified of the eligibility of nominations and specifically notified that, because of the fact that all nominations must be in the hands of the A.M.A. prior to the November 30, 1948, interim session of the A.M.A. House of Delegates, the selection of a possible nominee from California must be made by the Council and not by the House of Delegates.

Adjournment.

SIDNEY J. SHIPMAN, M.D., *Chairman.*
L. HENRY GARLAND, M.D., *Secretary.*

Marysville Postgraduate Seminar

The first autumn postgraduate seminar of the series being conducted by the Committee on Postgraduate Activities of the California Medical Association was held at Marysville, October 1. The program consisted of a morning clinical conference on nephritis conducted by Dr. Marcus A. Krupp of the Veterans Administration, San Francisco, with presentations of types of acute and chronic stages of the disease.

At the afternoon session, formal papers were read. Dr. Krupp presented the latest concepts of diagnosis and treatment of nephritis.

Dr. Rene Bine, Jr., of Mt. Zion Hospital, discussed the results of research investigations carried on in the University of California Hospital and Mt. Zion Hospital on the use of anticoagulants in the management of acute coronary disease. He stated that judicious use of Dicumarol and Heparin resulted in notable reduction in the complications of thromboembolic phenomena.

The management of allergic diseases was reviewed by Dr. Albert H. Rowe, University of California Medical School. Dr. Rowe's discussion and illustrative slides presented an excellent coverage of this very troublesome and confusing field of medicine. Hypersensitization and its varied manifestations were reviewed, and general and specific treatments outlined.

The evening session was a symposium on the management of common serious highway accidents, with three papers—"Internal Injuries to the Chest," by Dr. Paul Samson, assistant clinical professor of surgery, Stanford University School of Medicine; "Internal Injuries to the Abdomen," by Dr. Leon Goldman, associate professor of surgery, University of California Medical School; "Orthopedic Surgery: The Extremities," by Dr. Frederic Bost, associate clinical professor of orthopedic surgery, University of California Medical School.

Dr. Samson emphasized the importance of early, correct diagnosis and advocated conservative treatment pointed toward as rapid reestablishment of physiological relations as possible by early and repeated aspiration of hemothorax or hemopneumothorax; relief of severe intercostal nerve pain from severe fractures by judicious local blocking of the intercostal nerves rather than by unphysiological morphine sedation; restoration of lost blood; and, finally, decortication of organized clot and fibrin under proper conditions, four to six weeks after trauma, to favor reexpansion.

Dr. Goldman emphasized the importance of proper and adequate facilities for diagnosis and institution of early supportive therapy in injuries involving the abdomen. He listed as essential the Wangensteen suction apparatus, oxygen equipment, plasma and catheterization set-up, together with clinical and x-ray equipment and personnel to assist the emergency surgeon. Shock stages, important symptoms and the various organ systems were succinctly re-

viewed. Dr. Goldman said that radical surgical procedures are much more often requisite to proper handling of serious trauma to the abdomen than in thoracic injuries.

Dr. Bost reviewed the important orthopedic problems commonly encountered. His emphasis was upon proper early management of the complications of serious fractures. He warned against early introduction of foreign bodies in compound fracture reduction; and stressed debridement, immobilization, chemotherapy and antibiotic therapy together with proper physiological supportive and restorative management.

After these papers were presented two motion pictures were shown, "Compound Depressed Fracture of the Skull" and "Cholelithiasis with Common Duct Stone."

Attendance was 24 at the morning session, 50 at the afternoon meeting, and 31 in the evening.

Additional seminars are scheduled as follows:

Sunday, Nov. 7	Redding	Gastric Surgery, Obstetrical Difficulties, Myocardial Infarction and Psychosomatic Medicine
Tuesday, Nov. 9	El Centro	Gastro-intestinal Symposium including Biliary and Liver Diseases
Saturday, Dec. 4	Santa Barbara	To be announced
Tuesday, Dec. 7	Riverside	To be announced
Friday, Dec. 10	Monterey	Anemias — Maxwell M. Wintrobe, M.D., University of Utah.

In Memoriam

HANSEN, PAUL SCOTT. Died in Santa Barbara, September 26, 1948, aged 38, of poliomyelitis. Graduate of Northwestern University Medical School, Chicago, Illinois, 1938. Licensed in California in 1946. Doctor Hansen was a member of the Santa Barbara County Medical Society, the California Medical Association, and the American Medical Association.

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MELLINGER, WILLIAM J. Died in Santa Barbara, August 28, 1948, aged 61, of coronary thrombosis. Graduate of the Chicago College of Medicine and Surgery, Illinois, 1913. Licensed in California in 1919. Doctor Mellinger was a member of the Santa Barbara County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

REICH, WILLIAM WALTER. Died in Berkeley, September 19, 1948, aged 48, after a heart attack. Graduate of Stanford University School of Medicine, Stanford University-San Francisco, 1929. Licensed in California in 1929. Doctor Reich was a member of the Alameda County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

TILLMANNS, CARL SAMUEL JONATHAN. Died in Los Angeles, September 14, 1948, aged 65. Graduate of the Washington University School of Medicine, St. Louis, Missouri, 1907. Licensed in California in 1919. Doctor Tillmanns was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

CONTRA COSTA

Dr. George Degnan, member of the staff of the Contra Costa County Hospital, has been appointed acting medical director. Dr. Degnan is serving in the post vacated by the resignation of Dr. E. A. Merrithew who had been director for 35 years.

LOS ANGELES

Dr. C. Leonard Huddlestone, director of the department of physical medicine at the University of Southern California, was installed as president of the American Congress of Physical Medicine at a recent meeting of that organization in Washington, D. C.

* * *

Postgraduate medical courses in the control of infectious diseases will be held during the fall and winter months under the auspices of the Los Angeles City Health Department. The meetings, which are to be held in the State Building at 217 West First Street from 8 to 10 p.m., Thursday evenings through March 31, 1949, are being administered by the Department of Infectious Diseases, School of Medicine, University of California at Los Angeles, and University Extension of the University of California. There is no enrollment fee.

The program of meetings already scheduled follows:

October 21: The Public Health Service in the Control of Communicable Disease. Leonard A. Scheele, M.D., Surgeon General, U. S. Public Health Service, Washington, D. C.

October 28: Diagnosis of Fevers of Unknown Origin. Albert G. Bower, M.D., clinical professor of public health and preventive medicine, College of Medical Evangelists.

November 4: Streptococcal Infections. James N. DeLamater, M.D., assistant dean, University of Southern California School of Medicine.

November 18: (a) Meningogoccal Meningitis. (b) Meningitis as a Complication of Communicable Disease. Albert G. Bower, M.D.

December 2: The Pneumonias—Diagnosis, Management, Complications. Roger O. Egeberg, M.D., clinical professor of medicine, School of Medicine, U.C.L.A.

December 9: (a) Diphtheria. (b) The Differential Diagnosis of Infectious Mononucleosis, Septic Sore Throat and Vincent's Angina. Albert G. Bower, M.D., and Louis J. Fisher, M.D., assistant clinical professor of medicine, College of Medical Evangelists.

December 16: (a) Enteric Infections. (b) Typhoid Fever and Bacillary Dysentery. Evelynne G. Knouf, M.D., associate clinical professor of medicine, College of Medical Evangelists, and assistant clinical professor of medicine, U.S.C. School of Medicine.

January 6: Brucellosis. Charles M. Carpenter, M.D., professor of infectious disease, School of Medicine, U.C.L.A., and Leon Rosove, M.D., assistant professor of medicine, U.S.C. School of Medicine.

January 13: (a) Pertussis. (b) Influenzal Meningitis. William P. Frank, M.D., instructor in medicine, U.S.C. School of Medicine, and Charles M. Carpenter, M.D.

January 20: Influenza. Thomas Francis, Jr., M.D., professor of epidemiology, School of Public Health, University of Michigan.

January 27: Measles, Mumps, and Chickenpox—Diagnosis, Treatment and Complications. William J. Mitchell, M.D., assistant clinical professor, U.S.C. School of Medicine.

February 3: Poliomyelitis. Albert G. Bower, M.D., Norman B. Nelson, M.D., assistant dean and associate professor of preventive medicine, School of Medicine, U.C.L.A.

PLACER

Dr. Saul Ruby, formerly of San Diego, has been appointed health officer of Placer County. Appointment of Dr. Ruby was advocated by Dr. N. A. Dubin, president of a recently created health board which serves in an advisory capacity to the county board of supervisors.

SAN FRANCISCO

The University of California Medical Center received a total of $49,426 in research grants from the National Foundation of Infantile Paralysis for the seven-month period ending December 21, 1947, according to a report by the Foundation.

Two grants were received. One, a grant of $43,090, went to support work under the direction of Dr. Karl F. Meyer, director of the Hooper Foundation for Medical Research, to determine how polio virus and similar disease infections spread. Development of dependable and rapid tests for identification of the virus and diagnosis of the infection is another aim. The second grant, of $6,336, was made to the Medical School for the continuation of instruction in physical therapy.

* * *

As part of a drive to interest girls in a career of nursing, the Woman's Auxiliary to the San Francisco County Medical Society has awarded its first nursing scholarship to Lily Chin, an American girl of Chinese descent. She was chosen from among a large group of candidates because of an excellent scholastic record and an earnest ambition to become a nurse. She chose to take her training at the University of California School of Nursing. The scholarship pays her tuition for a three-year course.

* * *

Three new appointments to the faculty have been announced by Dr. Loren R. Chandler, dean of the Stanford School of Medicine. Dr. Henry S. Kaplan has been appointed professor of radiology, Dr. Alfred E. Maumenee chief of the division of ophthalmology, and Dr. John A. Luetscher, Jr., associate professor of medicine.

Dr. Kaplan, formerly a radiologist with the National Cancer Institute, succeeds Dr. Robert R. Newell who is setting up a teaching and research program in biophysics. Dr. Maumenee, formerly a member of the faculty of Johns Hopkins Medical School, was appointed to take the place of Dr. Hans Barkan who retired from the Stanford faculty last year. Dr. Luetscher also is a former member of the faculty at Johns Hopkins.

SAN JOAQUIN

Dr. H. S. Chapman, city physician for Stockton, last month resigned that post after 28 years' tenure. The resignation was accepted "with regret" by the city manager, who said that it would become effective when a replacement for Dr. Chapman could be found.

At the first two of eight scheduled meetings in the tenth annual fall series of the Stockton Postgraduate Study Club, Dr. R. Wartenberg, associate clinical professor of neurology at the University of California, spoke on Neurological Examinations in the Office, and Dr. Salvatore P. Lucia, professor of medicine at the University of California, discussed Common Blood Disorders—Indications and Contra-indications for Splenectomy. Dr. Henry Risford was chairman of the first meeting, Dr. Neill P. Johnson of the second.

Program for the remainder of the series as announced by Dr. C. A. Broaddus, chairman of the program committee, follows:

October 16: Dr. Frederick L. Reichert, professor of surgery at Stanford School of Medicine, "Treatment of Conditions Involving the Sympathetic Nervous System." Dr. Emil J. Gough, chairman.

October 21: Dr. Charles E. McLennon, professor of obstetrics and gynecology at Stanford School of Medicine, "Clinical and Roentgen Pelvimetry." Dr. Lauren L. Heston, chairman.

October 23: Dr. Carleton Mathewson, Jr., professor of surgery at Stanford, "Present Status of Vagotomy." Dr. W. T. Auld, chairman.

November 18: Dr. J. K. Lewis, "The Heart Clinic." This, the only clinical meeting of the series, will be held at the San Joaquin General Hospital. Dr. Louis Armanino, chairman.

December 9: Dr. Daniel G. Morton, "The Use of Endocrine Products in Obstetrics and Gynecology." Dr. E. P. Halley, chairman.

December 16: Dr. Claude S. Beck, professor of neurosurgery at Western Reserve University School of Medicine, "Surgery of the Heart with Special Reference to Revascularization." Dr. Broaddus will be chairman of this meeting which is also the annual meeting of the Study Club.

SAN LUIS OBISPO

Bubonic plague in pools of fleas taken from squirrels in the areas of San Luis Obispo County has been demonstrated in tests at the state laboratory, according to a report by the California Department of Public Health.

SONOMA

With public contributions lagging, members of the Sonoma County Medical Society plan to provide about $8,000 to underwrite the proposed Sonoma County Community Blood Bank. It was announced by the Society that members would contribute $100 each to help in setting up a locally controlled blood bank. This decision was reached at a meeting of the Society at which Dr. John Upton, chairman of the Blood Bank Commission of the California Medical Association, outlined the problems of establishing a community bank. Dr. Upton said that San Francisco, San Mateo and Sacramento had been successful in setting up locally controlled blood banks.

Agreement of the members of the Society to subscribe $100 per member followed revelation that only about $3000 of $25,000 sought for the project had been raised by public contributions. The Society said that although members' contributions would be made with the understanding that refunds might be expected if public subscription ultimately provided sufficient funds, the members are prepared to leave their money in the fund if necessary.

TULARE

Dr. Adolph Wallner of Van Nuys has been named director of the Tulare County Hospital to take the place of Dr. Austin Miller.

YUBA-SUTTER-COLUSA

A seminar held October 1 in Marysville under the direction of the Committee on Postgraduate Activities of the C.M.A. was "highly praised" by those who attended, according to a report received from Dr. Leon M. Swift, secretary of the Yuba-Sutter-Colusa County Medical Society. Several physicians from surrounding communities as well as members of the local society attended, it was reported.

GENERAL

A new booklet stating the new and revised morbidity reporting requirements of the U. S. Public Health Service, with instructions and samples of report forms, has been issued by the Federal Security Agency. The new reporting requirements, the FSA said, were set up in an effort to bring about uniformity and simplification in morbidity reporting. Copies of the booklet may be had from Federal Security Agency, Public Health Service, Division of Public Methods, Washington 25, D. C.

* * *

Physicians treating beneficiary members of California Physicians' Service have been given an extension of the time limit within which they may submit bills for payment. Formerly 90 days after the end of the month in which services were rendered, the time for submission of bills now has been increased to six months. The improving financial position of C.P.S. warrants the time extension, according to Dr. Chester L. Cooley, secretary of the C.P.S. board of trustees, who explained that the 90-day rule was put into effect at a time when it was necessary to keep closer abreast of the liabilities represented by bills for services rendered.

Bills submitted to C.P.S. more than six months after the end of the month in which the service was rendered cannot be paid, the announcement said. Physicians were urged not to wait until the end of a course of treatment to submit a bill to C.P.S., but to send a bill at the end of each month for the treatment given within that month.

The time extension applies only to medical care rendered after October 1, 1948. Bills for services that were performed before that time must be sent to C.P.S. within 90 days of the end of the month within which the service was rendered.

* * *

"Gastric Cancer" is to be the subject for discussion at a special dinner meeting to be held on December 13, at the Fairmont Hotel, at 6:30 p.m. The meeting is sponsored by some of the county medical societies in the San Francisco Bay Area in conjunction with the Gastric Cancer Committee of the National Advisory Cancer Council. The speakers and their subjects are:

Dr. John A. Morton, professor of surgery, University of Rochester, Rochester, New York, "New Horizons in Gastric Cancer."

Dr. George N. Papanicolaou, professor of clinical anatomy, Cornell University, New York City, "Exfoliative Cytology as Applied to Gastric Cancer."

Dr. Leo Rigler, professor of radiology, University of Minnesota, Minneapolis, "Radiology in the Gastric Cancer Problem."

Reservations can be made by sending a check for the cost of the dinner ($5.50) to Dr. Ralph T. Behling, Cancer Control Officer, District No. 5, U. S. Public Health Service, 237 Federal Office Building, San Francisco 2, California.

* * *

The seventh annual meeting of the American Academy of Dermatology and Syphilology will be held in Chicago from Saturday, December 4 through Thursday, December 9, it is announced by Dr. Earl D. Osborne, secretary-treasurer of the Academy. The principal session will be held at the Palmer House, with special courses in histopathology and mycology scheduled for Saturday and Sunday, December 4 and 5, at

the Medical Schools of the University of Illinois and Northwestern University. As in the past two years, teaching clinics will be held on the afternoons of Monday, Tuesday, and Wednesday, December 6, 7, and 8. A new feature is being added to the program this year consisting of informal discussion groups which meet at noon and 5:00 p.m. sessions. Special courses in histopathology, mycology, x-ray and radium therapy, mucous membrane lesions, bacteriology of the skin, industrial dermatoses, specific granulomata, and dermatoscleroses will be held under leaders in these various fields.

* * *

From a recent analysis of 100,000 surgical benefit claims of all ages made by a committee of the Actuarial Society of America, the *Connecticut State Medical Journal* has excerpted "a number of interesting statistics," which it reports as follows:

"Not all surgery is performed in hospitals: 2 per cent of operations on men were performed out of the hospital; 16 per cent for children; and 11 per cent for women.

"The average amount paid for out-of-hospital claims was less than one-third that for hospital surgery.

"It was found that for an appendectomy 30 per cent of the doctors charged less than $100; 50 per cent, less than $125; 80 per cent, less than $150; and 90 per cent, less than $165. Charges were generally higher for men employees than for women, thus reflecting the general practice of suiting fees to the ability to pay.

"Surgical fees were highest on the West Coast, with California leading. They were next highest in the Middle Atlantic states and lowest in the South Atlantic states. Eight operations accounted for most of the surgical claims. These were: tonsillectomy, appendectomy, benign tumor or cyst, hemorrhoidectomy, fracture, hysterectomy, herniotomy, and dilation of curettage."

* * *

Eighteen outstanding medical teachers have been selected for the first Annual Scientific Assembly of the American Academy of General Practice to be held in Cincinnati, March 7, 8, and 9, according to announcement by the program committee. The names of the essayists and their subjects will be announced later.

Arrangements have been made to accommodate more than 2,000 members and their wives. Non-members of the Academy may attend the Assembly as guests on payment of a registration fee of $5. Only doctors of medicine may register. There will be no registration fee for members. A printed form for requesting hotel accommodations will be sent to all members later, the announcement said.

* * *

A meeting of the American Goiter Association will be held May 26-28 at Madison, Wisconsin, according to a recent announcement by the association.

* * *

Construction of a new 1,000-bed psychiatric hospital at Fort Funston, San Francisco, to serve veterans in Northern California is expected to get under way next year, the Veterans Administration reports. Acquisition of 200 acres of the military post for the hospital has been approved by the Administrator of Veterans' affairs.

* * *

Approximately 400 U. S. cancer control leaders are expected to attend the first annual National Cancer Conference, February 25-27, 1949, to be held in Mephis. The conference will be sponsored jointly by the American Cancer Society and the National Cancer Institute of the Public Health Service. Various phases of the cancer problem will be discussed at round-table forums. Participants will include outstanding doctors and scientists from all parts of the country in the fields of medicine, nursing, statistics, research and public health.

The Medical Faculty of the University of California will offer the following program of postgraduate courses for qualified physicians in 1949:

January 31 through February 4, all day

Psychiatry for General Practitioners. A course intended to give the general practitioner some knowledge of the major psychoses, with discussions of what he should do when he sees such cases. The general concept and treatment of psychoneuroses will be discussed. The integration of psychiatry with other fields of medicine will be considered, and some of the material commonly known as psychosomatic medicine will be offered.

January 31 through February 4, all day

Cardiology. This course will cover some recent advances in the knowledge of diseases of the cardiovascular system, with clinical demonstrations and discussions.

In addition there will be evening sessions during the same week, on Interpretation of Electrocardiograms. These evening sessions will constitute a separate course and can be taken separately or as a supplement to the course in Cardiology.

June 20 through 24, all day

Endocrinology, Including Diabetes. In this course emphasis will be placed on the clinical aspects, with instruction regarding diagnosis and management of endocrine diseases.

July 5 through 8, all day

Obstetrics and Gynecology. This course will be offered to all physicians interested in this branch of medicine. An attempt will be made to cover those things which are important from a practical point of view, as well as to include some of the newer points of interest.

September 5 through 9, all day

Otorhinolaryngology. This course is a continuation of the course offered in 1947, and is intended for specialists.

September 12 through 16, all day

Ophthalmology. This is a continuation of the course offered in 1947 and 1948, and is intended for specialists.

September 19 through December 5, every Monday evening

Continuation Course in General Medicine. This is a series of evening lectures for general practitioners. There will be twelve meetings of two hours each.

December 5 through 9, all day

Diseases of the Chest. Offered by the American College of Chest Physicians.

* * *

A national medical public relations conference, first of its kind, which will consider six issues facing the medical profession will be held in St. Louis November 27, Dr. George F. Lull, secretary-manager of the American Medical Association, announced. Public relations directors, executive secretaries charged with public relations duties and public relations committee chairmen from each of the 48 state medical societies will be invited. Carefully-selected discussion leaders from the state societies will grapple with these six major social issues facing the medical profession: selling the need of public relations to state medical society members, encouraging wider use of medical pre-payment plans, setting up workable systems for handling night calls, the rebate problem, developing good-will with labor, farm, industrial and co-op groups, and cooperating with health agencies.

The conference will immediately precede the annual secretaries-editors meeting, which is being held in conjunction with the annual Interim Session of the American Medical Association, November 28 to December 3.

INFORMATION

Summary of Information Regarding Some of the Newer Insecticides

The past few years have witnessed intense research in the development of new insecticides with resulting products such as DDT, DDD, chlordane and others which have proven to be a boon to the agricultural industry. However, these new compounds, besides being effective insect killers, are also toxic to humans and can be dangerous if improperly handled. Most recently a new group of compounds, the organic phosphates, has come into use and represents a potential threat to human beings.

Hexaethyl tetraphosphate (HETP) was developed in Germany and in that country was known as "Bladan." Tetraethyl pyrophosphate (TEPP), which is the active toxic ingredient in HETP, was independently developed at the University of Chicago a short time ago. Both these compounds are heavy, syrupy liquids freely miscible with water. On contact with moisture they readily hydrolyze and lose their toxicity; hence there is little residual action as in the case of DDT.

They are both extremely toxic to insects and animals, and very minute amounts (2-10 mgm/kgm) are fatal to experimental animals. Several cases of poisoning in humans have occurred in California and because of the increasing use of the compounds others will doubtless be reported.

Absorption—These products are freely absorbed from the gastro-intestinal tract following ingestion. In addition, experimentally, they are rapidly absorbed through the intact skin, a property which makes them extremely hazardous. They are only slightly irritating when first applied to the skin so that there is no immediate warning sign as to the potential danger. Instillation in the eye produces immediate local reaction. It is probable that they are also absorbed through inhalation of their vapors.

Pharmacology—HETP and TEPP act pharmacologically by causing an irreversible destruction of the enzyme cholinesterase. As a result of this action there is an accumulation in the body of acetyl choline with consequent symptoms of excessive parasympathetic nervous stimulation, producing both muscarine and nicotinic effects.

Symptoms—Symptoms of acute poisoning with these compounds are primarily those due to parasympathetic stimulation. There is marked pupillary contraction and spasms of the eye muscles of accommodation which may persist for two or three days, resulting in blurred vision and inability to focus on distant objects. There is frequently a feeling of tightness of the chest and observers have noted dyspnea, bronchial spasm and pulmonary edema resulting from capillary dilatation and excessive glandular secretions in the bronchi and bronchioles. The smooth muscle of the gastro-intestinal tract becomes spastic, causing vomiting, constipation or diarrhea, and abdominal cramps. The central nervous system is affected, causing excitement and sometimes convulsions, frequently followed by central nervous system depression.

Death in acute poisoning may be due to any one of the following mechanisms:

1. Bronchial constriction and cardiovascular collapse.
2. Central nervous system stimulation and eventual depression.
3. Stimulation and eventual depression of neuromuscular junctions.
4. Accidents occurring as a result of the visual or mental impairment.

Information regarding chronic toxicity and cumulative action is both incomplete and inconsistent. Experimental animals receiving sub-lethal doses have survived with no residual damage, presumably because they were able to reproduce enough cholinesterase to replace the amount destroyed by the insecticide. However, further studies on this point are necessary.

Diagnosis—At the present time diagnosis of intoxication with one of these compounds depends mainly on an awareness of the syndrome and on a high index of suspicion in areas where these chemicals are being used. Any person who may possibly have come in contact with these insecticides, complaining of "blindness," blurred vision, tightness of the chest or any of the other symptoms mentioned should be suspected of suffering from acute intoxication with an organic phosphate. The laboratory finding of reduced cholinesterase in the plasma is confirmatory evidence.

Treatment—Atropine protects against, and counteracts, the central and autonomic nervous system disturbances caused by these phosphates. Therapeutic doses (0.1 - 0.5 mgm/kgm) protect experimental animals against 3 to 4 lethal doses. Curariform agents, especially the magnesium ion, protect the myoneural junction against the nicotinic effects. The most effective therapy is a combination of atropine and magnesium.

Prevention—Poisoning by these compounds can be prevented if proper attention is given to safe methods of handling them and if all persons concerned appreciate fully their extreme toxicity. All contact with the bare skin must be avoided and im-

From the California Department of Public Health.

pervious gloves must be worn when handling the compounds. If any of the material gets on the skin it should be thoroughly washed off with copious amounts of soap and water. Inhalation of TEPP and HETP dust, mists and aerosols should be avoided by use of a mask approved by the State Division of Industrial Safety. Workers should change clothes completely and bathe with soap and water after using the material. Contamination of food and tobacco of course should be avoided. Any exposed person developing symptoms should immediately be removed from the exposure and should be seen by a physician as soon as possible.

Bureau of Adult Health—Physicians are urged to report cases of poisoning from insecticides to the Bureau of Adult Health, 2002 Acton Street, Berkeley 2, California. The Bureau is compiling such reports to be used as a basis for study of the problem. The Bureau's personnel and facilities are available to physicians for assistance in the diagnoses of these cases.

Another organic phosphate which is coming into widespread use is Parathione. Since this compound differs somewhat chemically and pharmacologically from HETP and TEPP, it will be discussed in a future bulletin.

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Lion Roars Less Loudly

[*Reprinted from the New England Journal of Medicine.*]

The Comitia of the Royal College of Physicians, acting in a spirit of sweet reasonableness, has forwarded two resolutions to the minister of health, Aneurin Bevan, vociferous sponsor of the National Health Service Act of 1946. The first suggests that an act be brought in by the minister of health amending the National Health Service Act of 1946 by discarding full-time medical service by regulation. The second recommends a bill to make regulations affecting the National Health Service subject to special parliamentary procedure rather than to ministerial dictation alone.

Mr. Bevan, departing from his accustomed role, has apparently listened to the voice of the British Medical Association as expressed in its plebiscite of January 31, in which it overwhelmingly rejected the National Health Service Act as it was originally written.

He has now proposed his own modifications of the Act. In these he relinquishes a full-time service to be brought into effect by regulation and also modifies the proposal for a universal basic salary, limiting such salaries to three years, after which the practitioner may make his own decision whether to continue with salary and capitation fee, or to continue with a capitation fee as the sole source of income from practice. These new proposals represent a considerable willingness to compromise, since even his own party is not entirely in sympathy with them.

The Government, according to Mr. Bevan's parliamentary secretary, now recognizes that a full-time salaried service is incompatible with free choice of physician by the patient; more, it recognizes the importance of the principle of free choice of physician and therefore puts forward the compromise of payment partly by capitation fee and partly by salary. Further, although the buying and selling of public practices will still be forbidden, every doctor will be free to practice where he wishes, except in professionally overcrowded areas, and will have the right to choose his partner or assistant.

A few strands of democracy will remain in Britain's anchor line, although, as the *British Medical Journal** phrases it, "Mr. Bevan's machinery may provide that justice will be done, but we doubt whether it will make it possible that justice 'may manifestly be seen to be done.' "

A plebiscite on the amendments proposed by the Government indicates that approximately 64 per cent of the British Medical Association members still disapprove of the Act, with 36 per cent approving. Only 52 per cent, however, are against serving under the Act whether they like it or not, a majority so bare that further organized resistance seems impossible.

There is no question that, with Britain's peculiar genius for compromise, the doctors of England will now unite in an organized effort to make the new system effective.

*Editorial. Plebiscite, Brit. M. J., 1:791-793, 1948.

BOOK REVIEWS

CORRELATIVE NEUROANATOMY. By Joseph J. McDonald, M.S., M.D., Joseph G. Chusid, A.B., M.D., and Jack Lange, M.S., M.D., fourth edition, revised. 60 illustrations. University Medical Publishers, Palo Alto, 1948. $3.00.

This work, which is in outline form, comprises descriptions of the peripheral nerves and the automatic nervous system, the spinal cord and the brain. It attempts to establish correlations between the anatomy and physiology of these structures and the symptoms and signs encountered in many neurological syndromes. It also presents an outline for a neurological examination and a resume of data concerning electroencephalography.

This book is not a substitute for the standard textbooks on neurology. It should provide a means, however, of presenting to students certain bald facts around which can be built a substantial structure of useful knowledge. Its chief value will be to undergraduate students preparing for examinations and to candidates for state board examinations and American board examinations which demand a reasonable amount of neurological information.

* * *

DIAGNOSTIC PROCEDURES FOR VIRUS AND RICKETTSIAL DISEASES. First edition. Publication Office American Public Health Association, 1790 Broadway, New York City, New York. 352 pp., 20 illustrations. $4.00.

This volume has been prepared by a group of outstanding authorities and is designed to present "a collection of laboratory methods at present applicable to the diagnosis of virus and rickettsial disease in man." This aim has been most satisfactorily attained, the many complicated procedures being intimately described. No experienced laboratory worker should have difficulty in the establishment of the various techniques by following the outlines presented in this book.

The material is presented in 16 sections, each of which is introduced by a brief description of an infectious agent and the human diseases caused by it. Isolation of the virus or rickettsia, and immunological methods useful in the study of infected human beings are then considered in great detail. The subjects covered are psittacosis, lymphogranuloma venereum, trachoma, inclusion blennorrhea, variola and vaccinia, influenza, primary atypical pneumonia, mumps, poliomyelitis, encephalitis, rabies, herpes simplex, yellow fever, dengue, phlebotomus fever, and the rickettsial diseases.

The technical material will not be of great value to clinicians but the book should be read in part by all physicians. The excellent brief descriptions of viruses and virus diseases will be of interest. In addition, the extreme complexity of virus isolation and immunological diagnostic techniques is emphasized. Too often a request for "virus studies" is made by the clinician who has insufficient understanding of the magnitude of the laboratory investigation which he has suggested.

* * *

MODERN CLINICAL PSYCHIATRY. By Arthur P. Noyes, M.D., Superintendent, Norristown State Hospital, Norristown, Pennsylvania. Third Edition. W. B. Saunders Company, Philadelphia and London, 1948. $6.00.

This standard textbook of psychiatry has been brought up to date in a fairly satisfactory manner without changing its orientation or style of presentation in any significant degree. The author's approach is the eclectic one, which is admirable, but sometimes the reader is left without much direction regarding varying points of view. The recent advances in treatment have been adequately covered.

The method of presentation is formalized along traditional lines, and is particularly suited to the wants of the student who feels the necessity of strict classification of clinical syndromes. The amount of case material is adequate for illustrative purposes.

In all, the book is useful to the student or physician who desires a concise presentation of the psychiatric conditions to be seen in hospital practice, but relatively weak in its presentation of the minor reaction types which constitute the great share of psychiatric material seen by the internist and general practitioner.

* * *

THE TREATMENT OF MALIGNANT DISEASE BY RADIUM AND X-RAYS, BEING A PRACTICE OF RADIOTHERAPY. Ralston Paterson, M.C., M.D., F.R.C.S.E., D.M.R.E., F.F.R. Christie Hospital and Holt Radium Institute, Manchester. The Williams and Wilkins Company, Baltimore, 1948.

This is a practical and well written book on modern radiation therapy, compiled with the assistance of various authorities, including Margaret Tod, Meredith and others. It stresses the present method of treatment as used at the Radium Institute in Manchester, and is replete with data on the use of radium molds and needles, and radon implants. Diagrams of radium set-ups are shown, and radiographs of the actual placement of radium in different cases are reproduced.

The x-ray treatment of malignant lesions is also presented but not in as much detail as is accorded radium. Paterson apparently still prefers radium for many types of case which could now be treated with low voltage x-ray or contact x-ray in this country. Indeed, contact x-ray is but briefly considered. Radioactive isotopes are mentioned only in passing.

Unfortunately no statistics are given as to the results of treatment following his methods and the reader is referred for these to the reports of the Holt Radium Institute.

Paterson stresses careful positioning of the patient, and the importance of meticulous care in maintaining position for x-ray treatments. Casts of plaster or plastic are individually fitted. Markers are put in place and films taken to accurately center the lesion from various ports. The tumor may first be outlined with inactive radon seeds or by the introduction of barium! Back pointers and large protractors are used to direct the beams through the previously localized ports. Considerable detail is included in the chapter on field selection and volume dose.

Tables are included for radium dosage using various applicators, and practical rules for distribution and dosage are discussed. There is a chapter on making radium molds. All the detail, however, only emphasizes the need for first hand instruction and practice.

Paterson adds x-ray roentgen and gamma roentgens for total depth dose calculation, but notes that from a biological viewpoint they cannot be summated. He brings out the importance of the time interval in relation to the field size and dose. Many writers tend to mention this briefly, if at all, but it is extremely important for the end results. Paterson indicates that similar results may be obtained with many different techniques and that there are few hard and fast rules in roentgen therapy. However, he suggests certain general types of plan and tends to treat his cases according to one of these plans, for example: 1 day radical or palliative therapy, 4 day palliative, 8 day palliative, 8 day radical, 18 day, 32 day and indefinite period plans. In skin tumors, for instance, small lesions up to 3 cm. in size can be treated with 1750-2000 r in a single session, or by any one of the above

mentioned time intervals with appropriate change in total dosage. He does not stress the ultimate cosmetic benefit of protection in skin lesions.

He stresses the importance of the *tumor dose* instead of the total air r, or r on skin so often found in the radiological literature.

Although all of Paterson's methods are not universally accepted as ideal, he does present a thorough and clear summary of treatment as found to be most efficacious for his organization. The radium studies are particularly useful and seem better presented than the x-ray. The chapters on the uterus and breast seem less adequate than those on the skin and oral structures.

This book is well worth including in the library of every radiologist.

* * *

DISEASES OF THE EAR, NOSE AND THROAT. By William Wallace Morrison, M.D., Professor of Otolaryngology and Attending Otolaryngologist, New York Polyclinic Medical School and Hospital. Appleton-Century-Crofts, Inc., New York, 1948. $8.50.

While this book is written largely for the use of the undergraduate student and the general practitioner, it is worth a place on the shelf of the otolaryngologist. The simplicity and clearness of the descriptions show the result of the author's long teaching experience. The absence of color plates would seem to detract from the value of the book but the author's drawings illustrate to an unusual degree the subject matter so that color plates seem unnecessary.

The short chapter on history-taking is of especial value to the student.

The descriptions of operative technique and bronchoscopy are not very complete, but are adequate for the purpose for which the book is intended.

Among the new features which are of considerable value are the chapters on local anesthesia, vasoconstrictor drugs, antibiotics, audiometry, aero-otitis, endaural surgery, the use of radium in the nasopharynx, Meniere's syndrome, allergy, headaches and laryngotracheobronchitis. Many more new features with a complete description of all recognized procedures in the practice of otolaryngology make the book very much worth while.

* * *

VENOUS THROMBOSIS AND PULMONARY EMBOLISM. By Harold Neuhof, M.D., Clinical Professor of Surgery in Columbia University; Consulting Surgeon to Mount Sinai Hospital, Montefiore, Beth El, and Hackensack, N. J., Hospitals. Mt. Sinai Monograph No. 2. Grune and Stratton, New York, 1948. $4.50.

This monograph is based on the author's wide experience with venous thrombosis and pulmonary embolism at the Mount Sinai Hospital in New York City. It is divided into two parts. The first deals with various forms of venous thrombosis and pulmonary embolism, with illustrative case reports. Emphasis is placed on thrombectomy with vein ligation in the surgical treatment of this condition.

Although anticoagulant therapy is mentioned, it is not adequately described or discussed.

The second part of the book is devoted to an analysis of 88 proven cases of fatal pulmonary embolism which occurred in the period between January 1, 1928, and April 1, 1938. There are excellent clinical descriptions with a correlation of the postmortem findings. The author emphasizes the fact that "there is no constant relationship between the degree, location and extent of the pulmonary embolism and the clinical syndrome produced."

The chief value of this book lies in the clear description of the clinical cases of pulmonary embolism. It is recommended for those physicians who are particularly interested in the finer points in diagnosis and pathology of this condition.

HUMAN NUTRITION. By V. H. Mottram, M.A. (Cant.), formerly Professor of Physiology King's College of Household and Social Science, University of London. Williams and Wilkins Company, Baltimore, 1948.

Although Mottram's fascinating and interesting volume is small, it is one of the most important contributions on human nutrition available to English-speaking peoples. The book, a primer of nutrition, emphasizes the biochemical and metabolic values of food in maintaining the human economy in optimum condition. Man is what he eats, and Mottram indicates why.

There are interesting chapters on the fundamentals of dietetics where the functions of food are stressed and a plea made for a mixed diet—one which will ensure the necessary elements for growth, maintenance, and repair. The chapter on digestion and metabolism presents the physiology of these important processes with simplicity and clarity. There is an excellent discussion of the *biologic value* of proteins, and the part they play in nutrition. The chapter on the importance of mineral elements is extremely practical. In another chapter the *optimal diet* is discussed in great detail from both the experimental and theoretical viewpoints. There is an informative chapter on cooking and processing of foods and how these factors influence nutritive value. Another chapter devoted to an exploration of the lore of meal habits shows the relationship between the time of taking meals and maximum muscular efficiency.

The last chapter of the book, dealing with the nature of foods, is a classic and should be read by everyone. It is a valuable book for the physician, and it is delightful reading.

* * *

PRINCIPLES GOVERNING EYE OPERATING ROOM PROCEDURES. By Emma I. Clevenger, R.N., Supervisor Eye Operating Room, New York Eye and Ear Infirmary, New York City. The C. V. Mosby Company, St. Louis, 1948. $5.50.

This book is well done and covers the field thoroughly. It follows the pattern of the methods used at the New York Eye and Ear Infirmary.

The book gives all procedures before, during and after operations on the eye. Part III, enumerating eye operations and the instruments used, is very instructive.

This book should be a must for any hospital having a department of ophthalmology. Both nurses and doctors can greatly benefit by reading it.

* * *

TUBERCULOSIS, A Discussion of Phthisiogenesis, Immunology, Pathological Physiology, Diagnosis, and Treatment. By Francis Marion Pottenger, A.M., M.D., Emeritus Professor of Medicine, University of Southern California, The School of Medicine. Illustrated. The C. V. Mosby Company, 1948.

Dr. Pottenger, an elder statesman among chest physicians in California, presents in this book his views concerning many aspects of tuberculosis. Adequate references are made to the literature for general orientation, but the emphasis is on Dr. Pottenger's own views and contributions.

The chapters on pthisiogenesis are confusing, containing vague references to toxins, enzymes, cellular excitation, general body excitation, etc. The known facts concerning the immune response to tuberculosis are not clearly presented, and the important contributions of Rich, Raffel, and others are virtually ignored.

The most unusual feature of the book is its emphasis on visceral neurology in relation to tuberculosis. Dr. Pottenger has made important contributions to this subject, and his detailed presentation of signs and symptoms caused by involvement of the vegetative nervous system is worth reading. To most physicians, the interpretation placed upon minor alterations in palpation and percussion will seem

somewhat esoteric. To quote one example: "Palpation and percussion showed enlarged hilum structures on both sides, with slight infiltration in both apices, more marked on the right. The right side showed considerable lagging and the apical muscles on both sides were slightly degenerated, and also in spasm. The apical process, however, did not seem to be sufficiently active to account for the symptoms."

Treatment is dealt with in a conventional manner, although Dr. Pottenger's enthusiasm for tuberculin therapy will not be shared by all.

For the student interested in a clear, objective orientation in the field of tuberculosis, this book cannot be recommended; the recent works of Rich and of Pinner are much more suitable. However, for the specialist who is acquainted with the literature and able to form his own judgments, Dr. Pottenger's viewpoint will prove stimulating.

* * *

HUTCHISON'S FOOD AND THE PRINCIPLES OF DIETETICS. Revised by V. H. Mottram, M.A. (Cant.). Sometime Fellow of Trinity College, Cambridge, and Late Professor of Physiology at King's College of Household and Social Science, University of London, and George Graham, M.D. (Cant.), consulting physician to St. Bartholomew's Hospital. Tenth edition. The Williams & Wilkins Company, Baltimore, 1948. $6.75.

This is an encyclopedic volume dealing with the biochemical and nutritive value of foods and the physiology of digestion and metabolism. The first five chapters of Section I deal with the subject of diet in normal life, and cover the fundamental divisions of the field of nutrition, namely those dealing with energy; body building materials; the minerals, with emphasis placed on the importance of the significant ones. There is an excellent chapter on the historical and evolutionary background of the vitamins.

The next four chapters are devoted to the practical aspects of nutrition, emphasizing the optimal diet and its availability and the processing, storage, cooking, and protection of foods. The section closes with two chapters devoted to the physiology of normal nutrition, where the topics of digestion, absorption, and metabolism in health are given in considerable detail. A short chapter on the subject of food habits closes the section.

Section II deals with the nature of foods. The chapter on foods used for energy is very good and contains an excellent discussion of the cereals and a detailed analysis of breads and the potato. Two chapters in this section are devoted to the proteins, which are presented from the point of view of their biologic value, eggs heading the list, followed by milk and milk products. Another chapter deals with the foods prominent because of their mineral and vitamin contents. A short chapter deals with the subject of flavors and condiments, and the last chapter with beverages—water, tea, coffee and alcohol. The latter is a dispassionate presentation of information on the subject which is aimed at dispelling the uncritical preconceptions of the clinician.

Section III is devoted to the clinical principles of feeding in infancy and childhood. The subjects of substitutions for human milk, and proprietary foods are covered in detail. Section IV deals exclusively with the clinical problems involved in the use of diet in disease. The discussions of diet in the treatment of fevers, obesity, and constipation are very good. The sections dealing with diabetes, arthritis, renal calculus and anemia could be improved. The topics of anorexia nervosa, gout, osteomalacia, peptic ulcer, gastrointestinal disturbances, sprue, cirrhosis, cardiac failure, epilepsy, and the nephritides are covered with reasonable adequacy. And the final chapter gives a critical analysis and evaluation of the problem of artificial feeding.

This book is highly informative and well written. The sections which deal with the fundamental subjects of chemistry, physiology and metabolism are among the best in the field, and they far overshadow the clinical sections. The bibliography is very well chosen, pertinent and good. The table of contents is unusually full and descriptive of the text and combined with the index makes the book extremely easy to use.

* * *

WAR, POLITICS, AND INSANITY. By C. S. Bluemel, M.D., The World Press, Inc., Denver, Colorado, 1948. $2.00.

The first chapters of this small book deal with an explanation of some psychological terms applied to personality, and a consideration of these personality traits as they appear in great personages of history, in particular the conquerors and dictators. The author's thesis is that rather than our choosing our leaders for desirable characteristics, they force themselves on us because of their aggressive and compulsive natures. The last chapters deal with a possible solution to this problem in a democracy. The whole work seems quite superficial, and seems to bear out very well the statement of Dr. Walter Schaller, that psychiatrists are spreading themselves so thin that even their patients are beginning to see through them.

* * *

ATLAS OF PLASTIC SURGERY. By Morton I. Berson, M.D., formerly director of the Department of Plastic and Reconstructive Surgery, the Downtown Hospital and Pan-American Clinic, New York City. Grune and Stratton, 1948. $15.00.

This is a book of 304 pages including the index. It begins with a diagrammatic representation of some of the procedures of plastic surgery and continues with short explanations of these various procedures as applied to the different parts of the body.

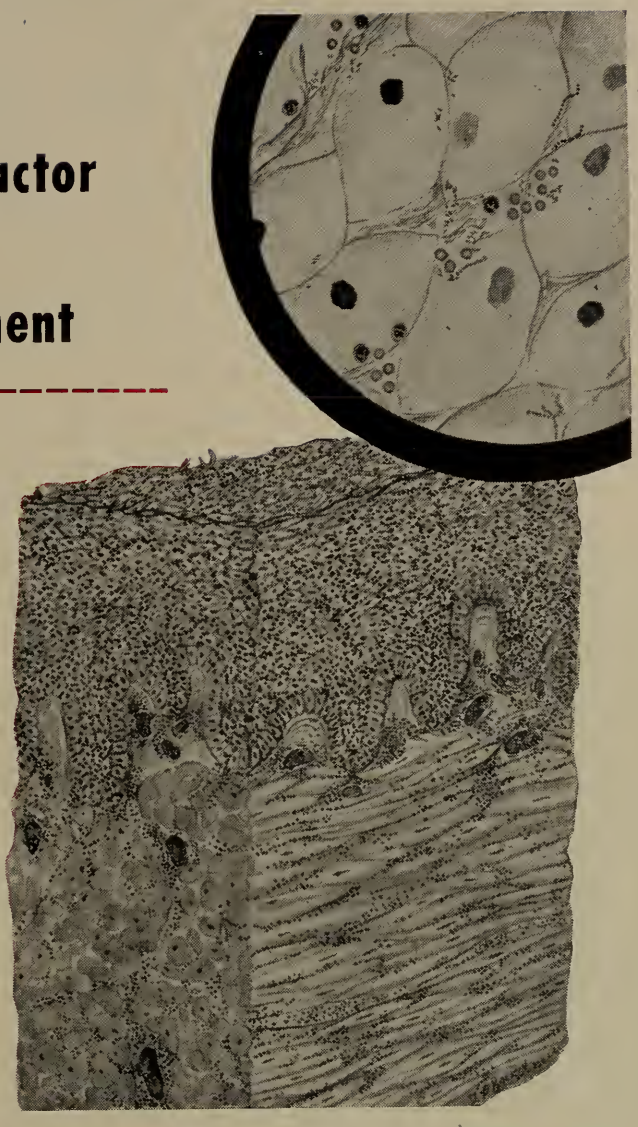
The text is very limited, as might be expected in an atlas, and often omits important factors in operation. The book is not well balanced in its attempt to cover the field of plastic surgery. For instance, six pages are devoted to reconstruction surgery of the hand and only four cases are illustrated. One of these is at fault in that a diagram of an already placed abdominal flap on the dorsum of the hand is shown in a drawing as completely dissected from the hand except at the line of the scar at the wrist. Such dissection would result in complete loss of this flap because blood supply would not be possible. In addition, the photograph of the final result in this case is taken at an angle instead of a full anteroposterior view so that the true result is not shown in the region of the webs of the fingers which, of course, it is supposed to illustrate. There are no illustrations or discussions of tendon surgery or nerve surgery of the hand. In comparison, there are 66 pages devoted to reconstruction surgery of the nose, the great majority of which illustrate so-called cosmetic surgery.

In a few illustrations of actual cases by the author there is a lack of final pictures. In reconstruction of the ear by the reviewer's method, as so captioned in the book, the author has missed some of the important steps in the operation and the reviewer does not like to be held responsible for the final result as shown in the photograph.

Of the two photographs of finished reconstruction of harelips showing repair of the original deformity, that of the repair of the bilateral cleft lip is utterly worthless as a photograph because it is badly out of focus or something has happened to the film so that the result cannot be seen.

For the untrained in plastic surgery too much is omitted and the problems are made to appear so simple that one would think he need only follow the diagrams of the Atlas to obtain easy results. The book will add nothing to the armamentarium of the trained plastic surgeon.

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*Boehme, E. J.: S. Clin. North America 25:545 (June) 1945.

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POWDERED ANTIBIOTIC DRUGS PREVENT LUNG INFECTIONS

Preoperative therapy with micropowdered penicillin and streptomycin is extremely valuable in preventing postoperative infections of the lungs, three physicians find from a study completed recently in the Departments of Medicine and Surgery, University of Rochester School of Medicine and Dentistry, and Dentistry and Clinics of Strong Memorial Hospital and Rochester Municipal Hospital, Rochester, New York.

Writing in a recent issue of *The Journal of the American Medical Association*, the physicians—George V. Taplin, Sidney H. Cohen, and Earle B. Mahoney—point out that prevention of lung complications following major abdominal or chest surgery is especially important in the northeastern sections of the United States where chronic sinusitis and chronic respiratory infection are found in a relatively large percentage of the population.

Postoperative lung infections occur following major abdominal or chest surgery in 18 to 20 per cent of cases in the Rochester, N. Y., area, they say.

Dr. Taplin is Associate Clinical Professor of Medicine at the University of California, Los Angeles. The other two physicians are at the University of Rochester School of Medicine and Dentistry and the hospitals where the study was made, Dr. Mahoney as Assistant Professor of Surgery and Dr. Cohen as Assistant Resident in Surgery.

Their work concerns only the types of lung complications caused by bacteria-infections such as bronchitis, bronchopneumonia, and partial collapse of the lung, with or without pneumonia, according to the article.

Use of penicillin and streptomycin in the micropowdered form is easier in the treatment of lung infections than administering the drugs in other forms, the physicians found.

The finely powdered products can be drawn into the respiratory tract by inhaling from a small cartridge. These small particles penetrate to the lungs so that they immediately reach the site of infection, the physicians say.

An analysis of 320 patients who received this form of penicillin shows that 5 per cent had allergic sore throat, consisting of redness, swelling, and, occasionally, blisters on the mouth and tongue. These local reactions subsided in two to five days after treatment, the physicians observe.

Forty patients were studied who received penicillin by atomizer or mist type aerosol—a fine mist—and a similar group of 51 patients was treated with micropowdered penicillin. The micropowdered form of streptomycin was given to 40 patients.

Twenty per cent of the patients who received penicillin by atomizer or aerosol had postoperative lung complications. The rate was 2 per cent for patients who received micropowdered penicillin, and none of the patients who received micropowdered streptomycin had postoperative lung complications. Further, cultures from patients who received the streptomycin showed in 25 per cent of the patients that there were no germs of any kind present in material taken from the throat and mouth after surgery.

Local penicillin reduced intranasal bacteria 99%

Proceedings of the Society of American Bacteriologists,
47th general meeting, May 13-17, 1947

A series of patients was treated intranasally with local penicillin, *500 units per cc.*, for 5 consecutive days. At the end of this time, the bacteria count was reduced from an average of 7,363 per cc. of nasal washings to the amazingly low average of 42.

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the penicillin-vasoconstrictor combination for intranasal use

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COHESIVE BANDAGE PREVENTS CLUB FOOT IN CHILDREN

(Continued from Front Advertising Section, Page 30)

For the newborn baby the bandage is reinforced daily and changed once a week, with more correction at each treatment. Since the deformity is corrected rapidly at an early age, it is important for parents to realize the necessity of continuing treatment until the child walks, according to Dr. Hauser. If treatment is stopped too soon, the deformity may reoccur, he says.

Although in some cases a tight tendon in the foot will not allow a full correction with the bandage alone, the tendon can be lengthened by surgery, he indicates. In only a few cases does the child fail to develop a normal foot.

PASTEURIZATION OF MILK PREVENTS UNDULANT FEVER

Pasteurization of milk and dairy products is the only practical method of preventing undulant fever, which affects 30,000 to 40,000 persons annually in the United States, points out Charles L. Steinberg, M.D., of Rochester, N. Y.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Steinberg reports:

"Pasteurization of milk and dairy products for human subjects is the only practical method available in view of the complex picture regarding the widespread existence of this infection in cattle.

(Continued on Page 40)

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Manufacturing Chemists

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PASTEURIZATION OF MILK PREVENTS UNDULANT FEVER

(Continued from Page 38)

"It is economic suicide and a practical impossibility to eradicate Bang's disease by slaughter of infected cattle. The accepted method of control of this infection in animals is by vaccination. Better dissemination of present-day knowledge and more research are needed."

Undulant fever is transmitted to human beings from infected livestock. In cattle the infection is known as "Bang's disease."

Undulant fever can cause arthritis of the sacroiliac joints of the lower back, Dr. Steinberg says, explaining that symptoms of the disease are so varied that patients often appear to be suffering from nervous exhaustion or a psychoneurosis.

"One may be able to list any symptom from headache to constipation and be able to fit the picture in with that of chronic undulant fever," he comments. "The typical fever is often likened to the initial phase of typhoid. Aches and pains in the joints are often noticed."

Medical history shows various forms of undulant fever—one which scarcely makes patients ill and another which causes extreme illness for weeks. Most patients are moderately sick over a long period of time; two years of treatment may be required. Nearly all persons who have undulant fever recover.





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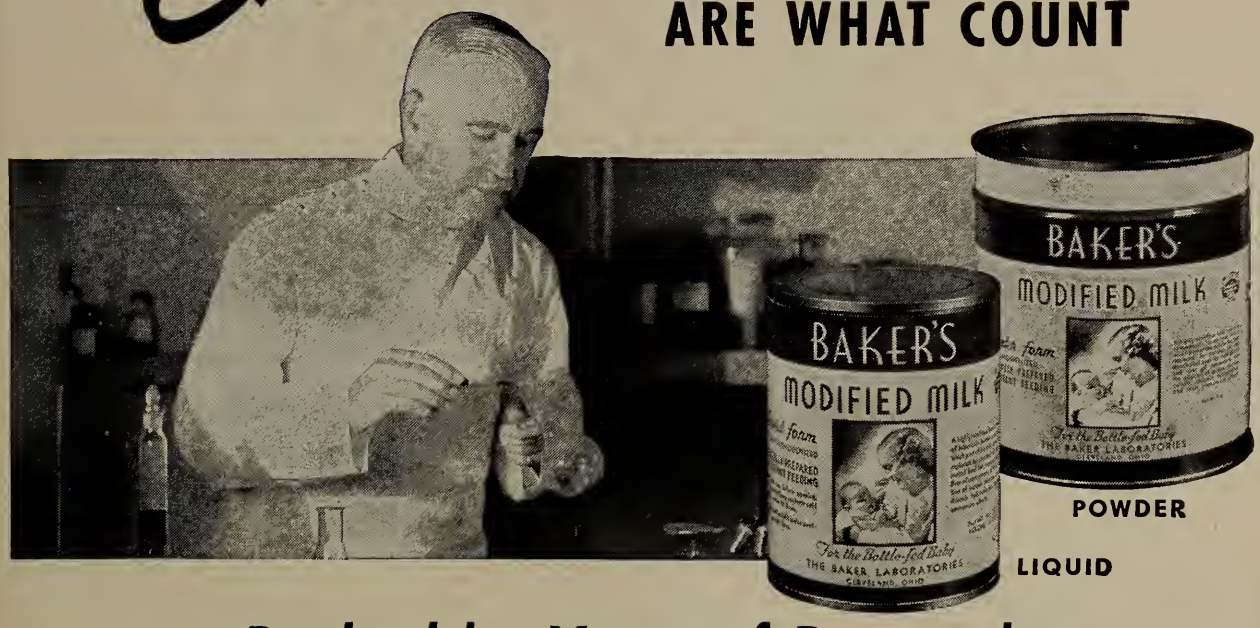


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RESEARCHERS DESCRIBE ARTIFICIAL KIDNEY

An artificial kidney developed by three researchers of Toronto, Canada, is saving the lives of persons whose kidneys do not function or function improperly.

The three researchers—Gordon Murray, M.D., Edmund DeLorme, M.D., and Newell Thomas—describe the apparatus in a recent issue of *The Journal of the American Medical Association.*

When secretion of urine stops following blood transfusions, certain conditions in pregnancy or poisoning, they say, toxic substances accumulate in the blood. Physicians formerly had little control over the condition, the researchers point out, and when it persists it is always fatal.

"It was with great satisfaction, therefore," the article continues, "that we were able to produce a machine which will reproduce the function of the kidney and will remove many, if not all, of the toxic substances that cause the fatal result."

The apparatus has been successfully used on patients and several days of treatment cause no ill effects, the researchers report.

The artificial kidney is the product of many years of work by these men, who began with attempts to transplant kidneys and to filter blood in animals. In its present form, they say, it operates by means of a cellulose membrane, which filters the blood, separating large particles from small ones.

This membrane is placed in a chemical bath containing sodium chloride, other chlorides, sodium phosphate, sodium carbonate, and dextrose, the article explains. A pump removes blood from the large trunk vein of the body which provides circulation to the legs and passes it into a tube, through the membrane, and into the opposite vein of the flank.

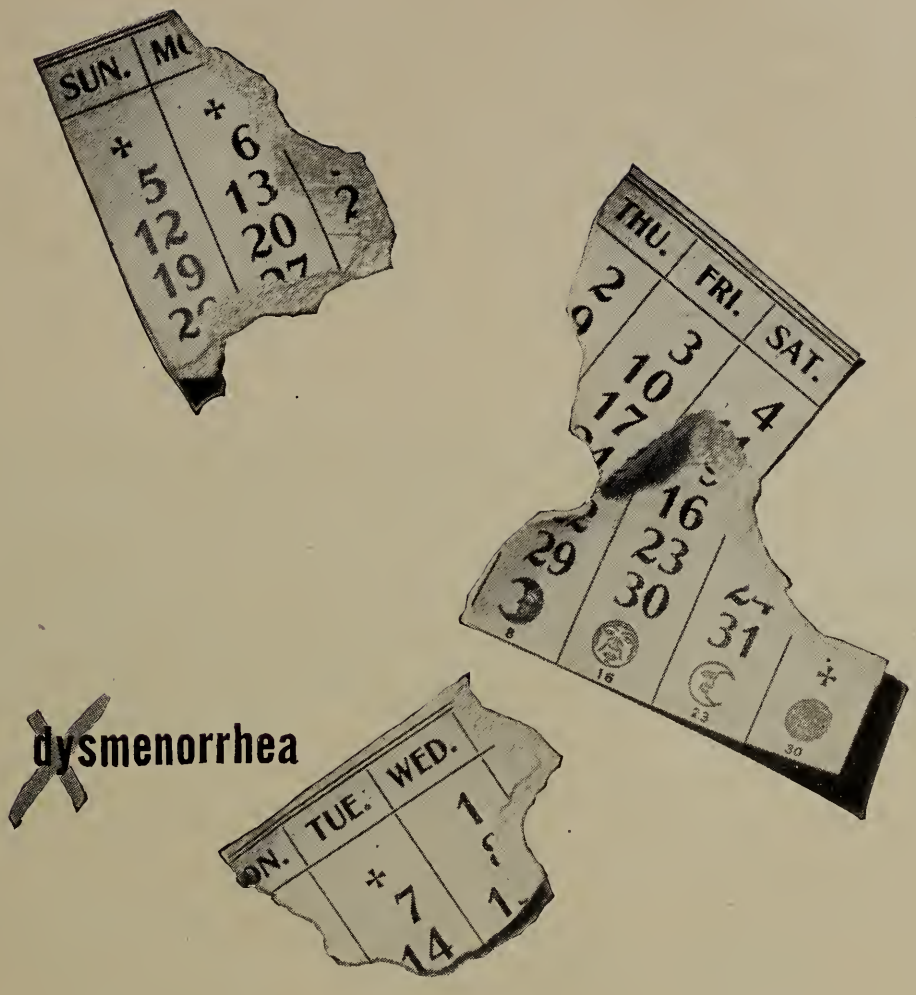
As the blood of a patient circulates through this route, the toxic substances fall out through small openings of the membrane. Large molecules such as proteins and hormones are carried back into the blood stream.

The substances which are filtered out plus sugar and water escape rapidly into the surrounding bath where buffering takes place—a chemical process which prevents alterations in the solution which would be harmful to the patient. By changing the solution frequently, the rate of filtration can be kept at a comparatively high speed, the researchers say.

Provided that the blood, both in the patient and as it enters the machine, is adequately treated with heparin, a drug which prevents clotting, the machine gives "no difficulty whatever," they observe.

Laboratory results point to further possible uses of the artificial kidney, the researchers indicate.

"Experimentally," they say, "we have demonstrated that when an animal is having a deficiency of oxygen a fairly large quantity of oxygen can be supplied by this machine. Moreover, the blood stream of the animal could be supplied with almost any desired quantity of sugar. There was evidence to suggest that various types of medication and treatment might be given for shock or severe burns."



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ROCKY MOUNTAIN SPOTTED FEVER SEVERE IN EASTERN STATES

The prevalence, severity, and high mortality of Rocky Mountain spotted fever in the Eastern states are not generally appreciated, say two physicians of Winston-Salem, N. C.

Writing in a recent issue of *The Journal of the American Medical Association*, the physicians—W. M. Kelsey and G. T. Harrell of the departments of pediatrics and internal medicine of the Bowman Gray School of Medicine of Wake Forest College and the pediatric service of the North Carolina Baptist Hospital—point out the following statistics:

In 1936, 50 cases of the disease were reported in Virginia and 32 each in North Carolina and Maryland, with mortality rates of 13.9, 14.1, and 25 per cent, respectively. In 1945 there were 99 cases reported in Virginia, 57 in North Carolina, and 47 in Maryland, with mortality rates of 20.1 per cent for Virginia and 31.7 per cent for North Carolina.

"It is probable that the actual incidence is much higher than the number of cases would suggest," they say.

Rocky Mountain spotted fever is a rickettsial disease—that is, it is caused by rickettsia, parasitic micro-organisms which are transferred to human beings by the bite of a wood tick or dog tick. It occurs most often in the spring and summer and among persons who work in the woods and fields.

(Continued on Page 49)

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ROCKY MOUNTAIN SPOTTED FEVER SEVERE IN EASTERN STATES

(Continued from Page 48)

Since only half the Rocky Mountain spotted fever patients treated by the two doctors remembered being bitten by a tick not long before the onset of the fever, contact with the tick required to produce the disease "may not be so long nor so intimate as is believed," the article emphasizes.

The incubation period, or time from the carrier tick bite to the onset of the disease, varies from one to eight days, say the doctors, and symptoms after the onset are high temperature, severe headaches, vomiting, and a rash.

Two types of specific therapy, hyperimmune rabbit serum and para-aminobenzoic acid, are available, according to the doctors.

"In our experience," they report, "hyperimmune serum has not proved to be of great value; large doses of serum have not yet been given an adequate trial, however. The value of para-aminobenzoic acid in Rocky Mountain spotted fever has not been definitely determined."

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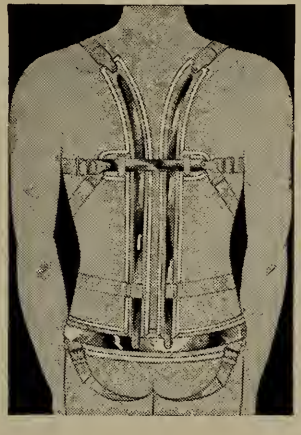


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REFERENCES:

1. Cooke, J. V.: Brennemann Practice of Ped. 4: Chapter 41, 1945.
2. Benson, R. A. et al: J. Ped. 31:369-754, 1947.
3. Sullivan, N.: Int'l Congress of Ped., Mt. Sinai Hospital, New York, 1947.

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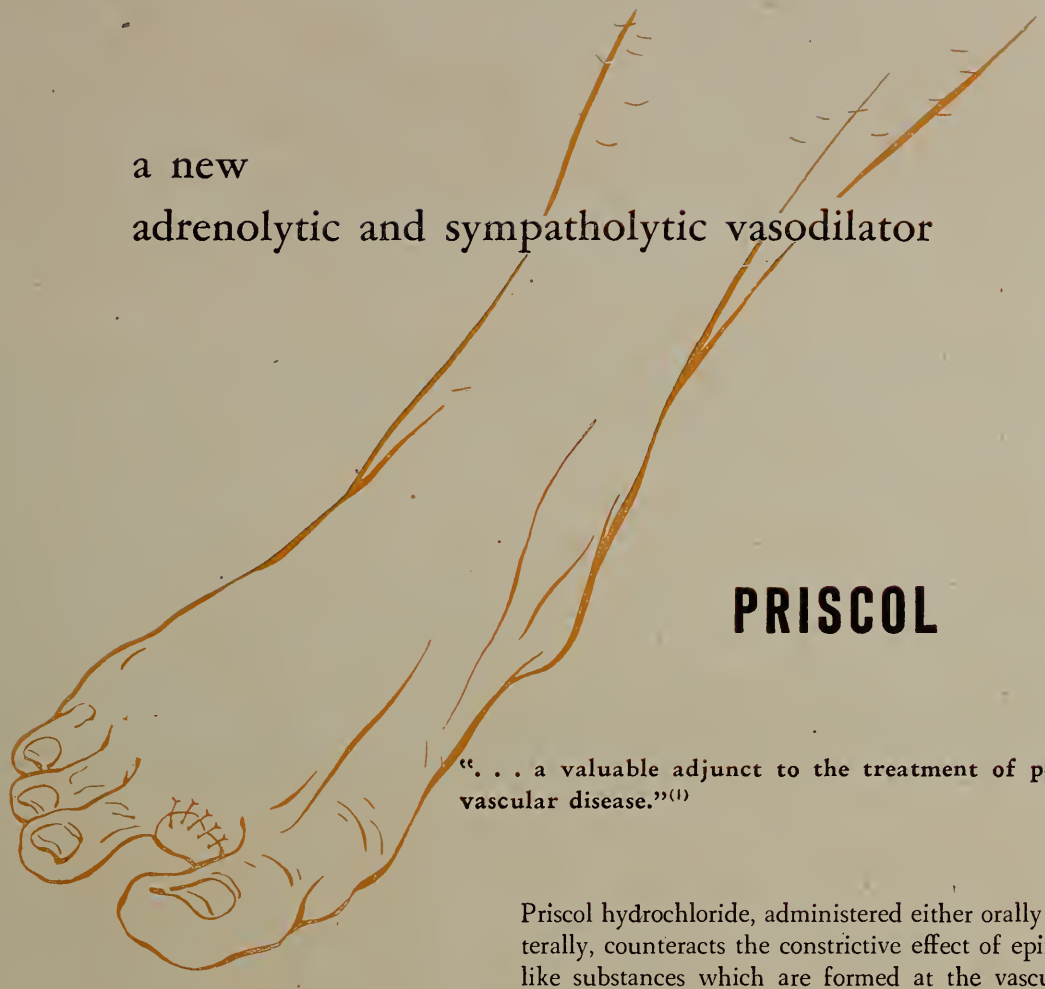
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Priscol therefore produces circulatory improvement in many cases of Raynaud's disease, Buerger's disease, diabetic gangrene, and arteriosclerotic peripheral vascular disease.

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Issued: Tablets of 25 mg.; bottles of 100 and 1000.
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1. Grimson, K. S., Marzoni, F. A., Reardon, M. J., and Hendrix, J. P.: *Surg.*, 23:728, 1948.

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DIPHTHERIA MORTALITY IN 1947 REACHES 200 FOR 93 U.S. CITIES

The number of diphtheria deaths in 93 large U. S. cities has decreased by 13 under the low 213 figure of 1941, according to the 23rd annual report on diphtheria mortality appearing in a recent issue of *The Journal of the American Medical Association.*

For the 88 cities for which data are available since 1923, there occurred 197 deaths from diphtheria in 1947, a new all-time low, the report states. This figure is 132 fewer deaths than 1946. The previous low was 209 deaths in 1941.

Of the entire 93 cities there was none with a rate in excess of 5.0 (there were three in 1946). This record was attained only once before in 1940. The number of cities with no deaths from diphtheria has increased from 30 in 1946 to 39 in 1947. The largest number (40) of cities found in this group was in 1940.

"In comparing 1947 with 1946 the significant decreases have occurred in the New England, South Atlantic, East North Central and West North Central cities," states the report. "Only the East South Central cities show an increase. Health officials continue to encourage protective treatments for infants and preschool children and recommend booster doses at time of school admission and later in life when

(Continued on Page 58)

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DIPHTHERIA MORTALITY IN 1947 REACHES 200 FOR 93 U.S. CITIES

(Continued from Page 52)

conditions indicate that it is desirable. Diphtheria can be eliminated through health education and parental understanding by extending programs for the protection of susceptible groups."

Nineteen cities—Bridgeport, Des Moines, Elizabeth, Erie, Fort Worth, Grand Rapids, Jersey City, Long Beach, New Bedford, Newark, Paterson, Peoria, Reading, South Bend, Syracuse, Utica, Waterbury, Wichita, and Yonkers report no deaths from diphtheria in 1946 and 1947.

The 18 cities (population 13,129,185) in the Middle Atlantic states continue to hold first place. The group rate is 0.24.

The 19 East North Central cities (population 9,386,378) are in second place with a group rate of 0.30 and 20 deaths among residents.

In third place are the nine cities of the West North Central states (population 2,716,484). There were eight deaths among residents in 1947, and the group rate is 0.41.

The nine cities of the South Atlantic states, population 2,727,985 (Charlotte is not included in this group), are in fourth place with a new low of 15 deaths and a rate of 0.55.

With 15 deaths in 1947 and a group rate of 0.58,

(Continued on Page 62)

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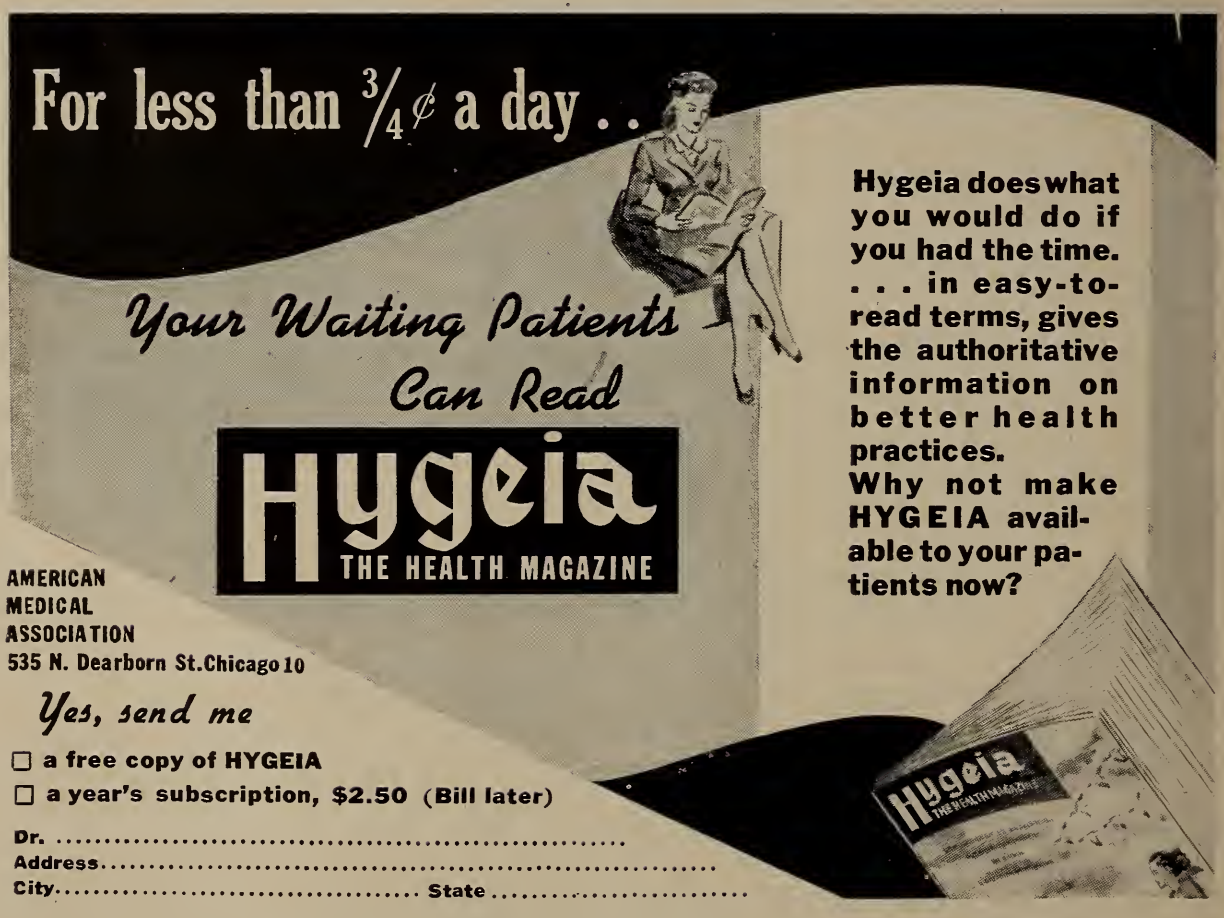
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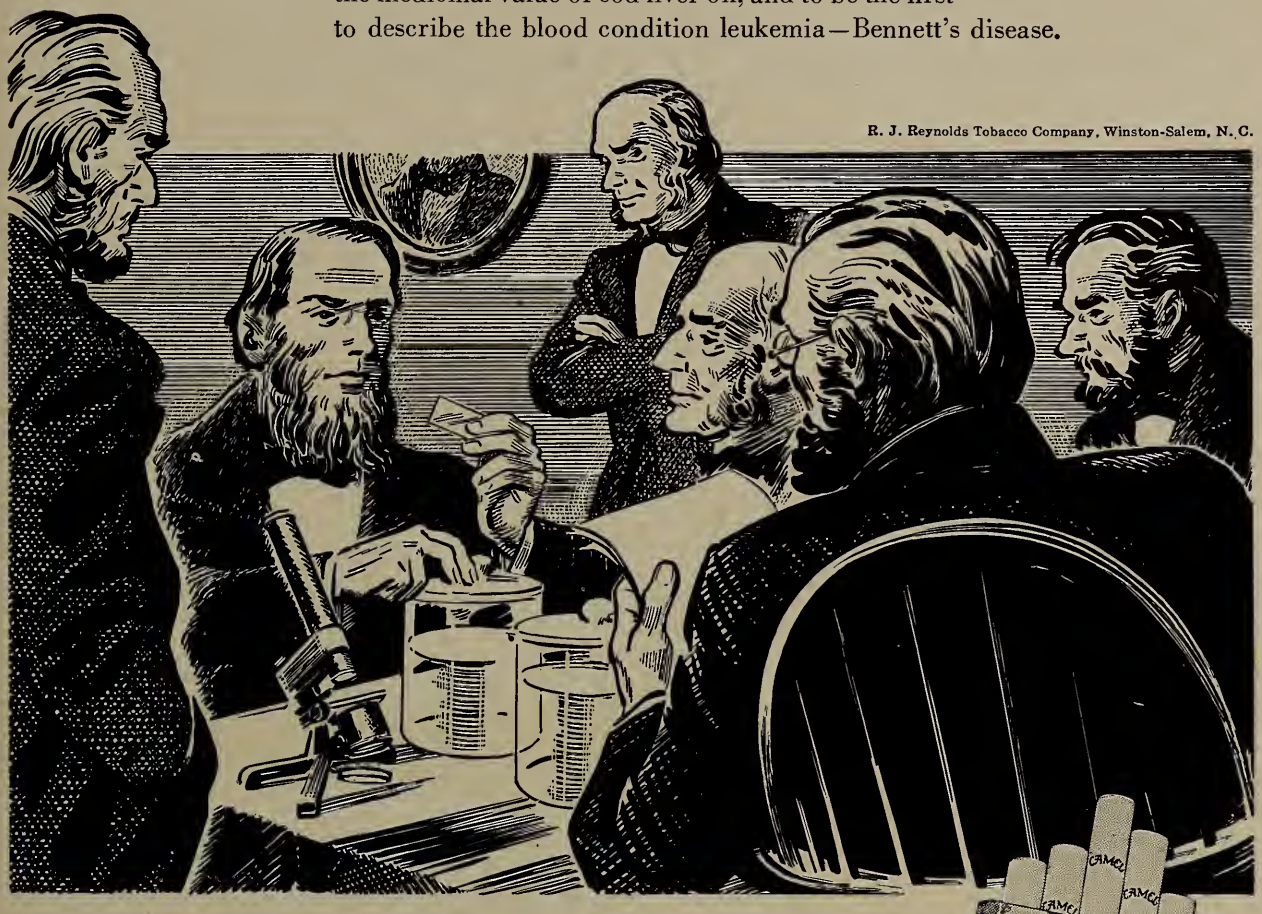
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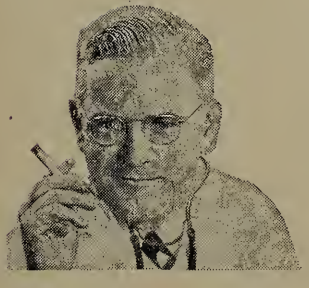
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DIPHTHERIA MORTALITY IN 1947 REACHES 200 FOR 93 U.S. CITIES

(Continued from Page 58)

the 14 New England cities (population 2,579,152) have failed to equal the low of six deaths (in 1940). These cities are in fifth place in 1947.

The eight cities of the West South Central states (population 2,048,692) report 11 deaths among residents. With a rate of 1.02 the group ranks in sixth place.

The six cities in the East South Central states (population 1,286,747) report an increase in deaths from diphtheria—nine among residents. The group rate is 1.31 and the cities are in seventh place.

The 11 cities (Sacramento is not included) in the Mountain and Pacific group (population 4,186,039) report a decrease in the number of deaths, although the cities are in eighth place. There were 61 deaths from diphtheria in these cities in 1947 and the rate is 1.45.

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ARMY SAYS 4,000 MORE DOCTORS NEEDED BY JUNE, 1949

In a letter appearing in a recent issue of *The Journal of the American Medical Association,* Major General R. W. Bliss, surgeon general of the Army, says that since the new Selective Service Act has established a peacetime army and air force at approximately five times the size of the prewar establishment, it is estimated that at least 4,000 more doctors will be needed by June, 1949.

"But the problem confronting the Army is not solely one of numbers," he said, adding: "We are still very short of specialists, despite our refresher training and our comprehensive postgraduate training."

General Bliss pointed out that while the Army, including the air force, must secure 4,000 doctors by next June, it cannot depend entirely on the group of young men who were permitted to complete their medical studies during the recent war and have as yet rendered no service to the government even though the majority of the group received liberal government stipends.

"After allowance is made for the attrition for physical disabilities and essential work, it is doubtful whether the remaining number would exceed 3,000. Of these, only about 2,000 will have completed a year's internship by June, 1949. It should be remembered that none of these 3,000 are obligated by any existing law for service for any period of time with the armed medical services," he said.

In an editorial appearing in the same issue of the *Journal,* the American Medical Association says that the men in the armed forces must have the highest possible quality of medical service.

Every possible approach to the problem of securing more doctors has been considered, the *Journal* editorial says, and now it appears obvious that "the first step is to make the service more and more attractive to the young men so as to encourage volunteering by greater numbers."

The *Journal* editorial says:

The House of Delegates of the American Medical Association established the Council on National Emergency Medical Service as a body to be especially concerned with meeting the needs of the nation for physicians in times of emergency. War today is total war. The needs of civilian populations and particularly of great industries, which are the backbone of war, must also be considered. Nevertheless, the men who do the actual fighting, who fly the planes, who get the foods and supplies up to the front and who carry the banner of the United States all over the world must have the highest possible quality of medical service in order to keep fit and efficient. The provision of the best medical care to our armed forces is one of the most economical steps that the nation can undertake. It lessens the total demand for men, and it maintains the morale and the spirit of the men more than any other single factor involved in modern war.

The Council on National Emergency Medical Service, the procurement divisions of our armed forces, the headquarters of the Army and Navy and Air

(Continued on Page 12)



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ARMY SAYS 4,000 MORE DOCTORS NEEDED BY JUNE, 1949

(Continued from Page 10)

Force have all been desperately concerned during the last few months with meeting the nation's need. Every possible approach to the problem has been considered. Now that compulsory service for physicians has been denied by the Congress, the needs must be met by other technics. Obviously the first step is to make the service more and more attractive to the young men so as to encourage volunteering by greater and greater numbers. A recent somewhat casual survey of the young men now in the service who will be leaving at the end of two years of service indicates that the following factors must be given consideration in attracting them for longer periods:

1. The service must be sufficiently varied so that the deadly routine of day by day dispensary service of many months does not destroy the young man's initiative.

2. At least one-half of the young men now in the armed forces want ultimately to qualify for certification by some specialty board. Some means must be found whereby service in military installations can be reckoned as a part of the young man's development leading toward certification.

3. Except in the most remote areas young men may be kept in contact with some of the best teach-

(Continued on Page 16)

The Colfax Hospital for the Tuberculous

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Bacitracin is supplied in 20 cc. rubber-stoppered vials containing 2,000 and 10,000 units, and in 50 cc. rubber-stoppered vials of 50,000 units; Bacitracin Ophthalmic Ointment-C.S.C. is available in ⅛ ounce tubes; Bacitracin Ointment-C.S.C. (for cutaneous application), in ½ ounce tubes. Both ointments provide 500 units of Bacitracin per gram. Literature available to physicians on request.

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ARMY SAYS 4,000 MORE DOCTORS NEEDED BY JUNE, 1949

(Continued from Page 12)

ers in American medicine. Already a steady stream of qualified consultants is visiting our Army hospitals throughout the world, and the men who are taking charge of the services in these hospitals are having more opportunity for extended contact with the leaders in the various medical specialties than most of the men who remain in the United States. All that appears to be needed is some arrangement for the development of a systematic course of instruction rather than the casual ward walks.

Thus most of the objections can be met by competent planning. While the young men prefer to be rotated from one service to another at fairly frequent intervals, several difficulties have developed in this regard. First is the housing of young men, many of whom are married and are already en route to the development of families. One colonel in charge of a hospital of many hundreds of beds in Germany said that there would be no problem for the Army medical department if all the young doctors would remain bachelors until they had completed their military service. The housing of young physicians and their families, as can easily be seen, is one of the most difficult of the problems that confront the armed forces.

(Continued on Page 17)

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ARMY SAYS 4,000 MORE DOCTORS NEEDED BY JUNE, 1949

(Continued from Page 16)

It has been suggested that increased pay in the armed forces for men as highly specialized as are physicians and engineers would attract more young men to the service. Actual first-hand surveys indicate, however, that the money, while interesting, is not a primary consideration.

A specific provision in the Selective Service Act states that a man may not be inducted into the armed forces until provision has been made for adequate medical care. That was the intent of the Congress. There is no reason to believe that the Congress will withdraw from that intent.

PENICILLIN AIDS IN TREATMENT OF TETANUS

Penicillin is a valuable aid in the treatment of tetanus, commonly known as lockjaw, according to three physicians of San Juan, Puerto Rico.

Writing in a recent issue of *The Journal of the American Medical Association*, the physicians—R. S. Diaz-Rivera, Luis R. Deliz, and Jose Berio-Suarez—describe a study of 59 patients who were treated for tetanus at the San Juan City Hospital.

Penicillin should be given with the tetanus antitoxin, they say. The mortality rate for all patients treated was more than 20 per cent, and the mortality rate of patients who were given enough penicillin to constitute a "fair trial" of the drug was nearly 18 per cent.

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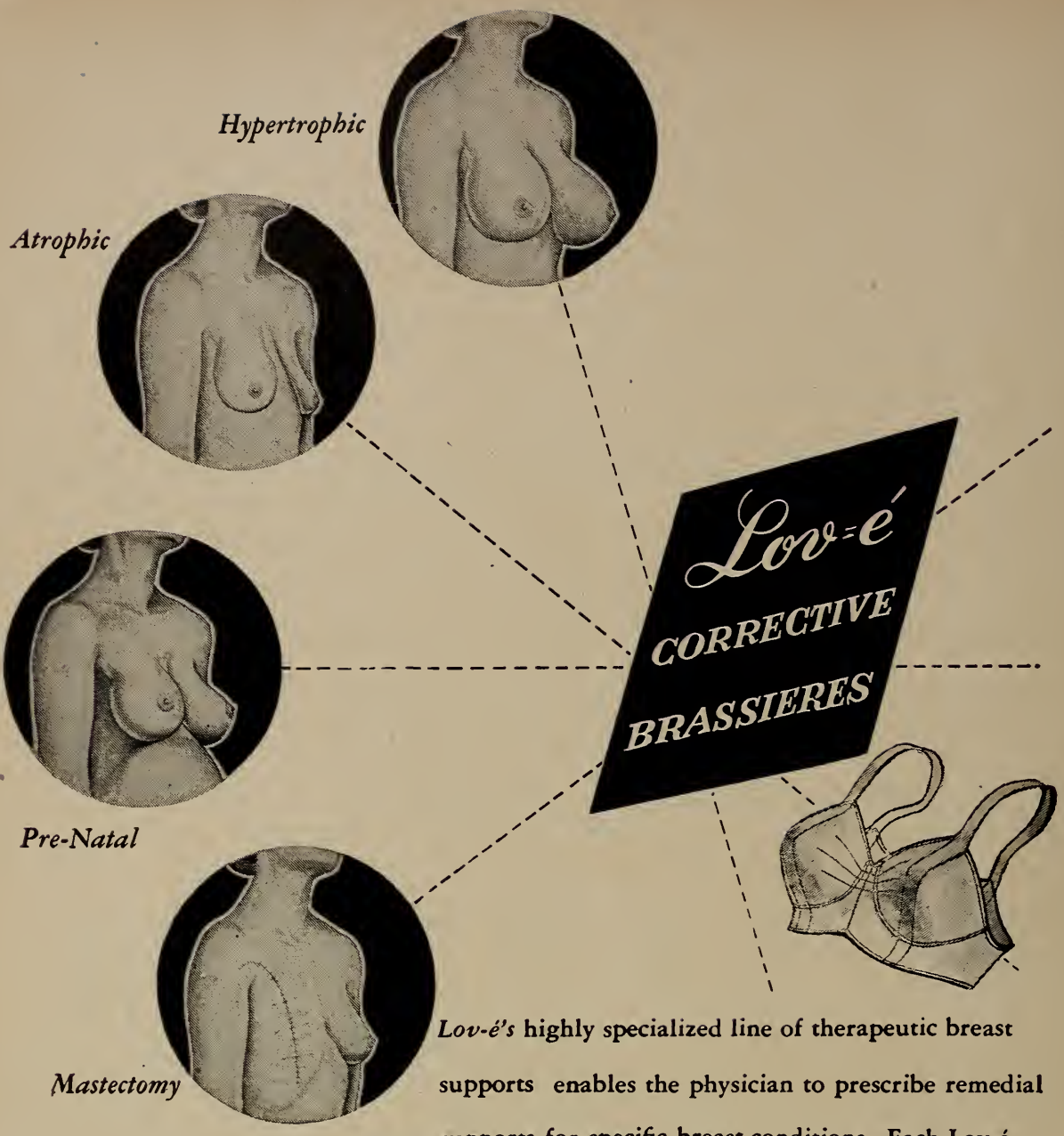
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ANTIVIVISECTIONISTS THREATEN MEDICAL RESEARCH

Sincere but misguided people who support antivivisection and the shrewd promoters who make a living from the movement are a real threat to medical research, points out an editorial which appears in a recent issue of *The Journal of the American Medical Association.*

The editorial follows in part:

"The antivivisectionists love publicity pointed to their angle, but screams of anguish and tearing of hair will soon be reflected in the anti-vivisectionist publications after the recent (July 24) article in the *Saturday Evening Post*, 'They're Trifling With Your Life.'

"This article designates the antivivisectionists as 'an obscure cult of sincere but misguided Americans —spurred by shrewd promoters—(which) now threatens to wipe out the techniques of medical research that have saved millions from horrible deaths.'

"The vast majority of antivivisectionists are apparently sincere but misguided. They are kindly people who love animals perhaps too well. Their noble sentiments make them easy prey to the shrewd promoter who makes his living by claiming that animals in laboratories suffer needless pain, and that money is needed to stop animal experimentation. The people who support the antivivisectionist movement have never been in laboratories and have only the vaguest concept of what constitutes scientific research.

"The combination of 'sentimental money,' as the gifts to antivivisectionism have been termed, plus shrewd promotion, embodies a real threat to medical research. Year after year the antivivisectionists have had bills introduced into the Congress of the United States and into state legislatures 'exempting' the dog from service in the medical research laboratory. Such bills, one of which came perilously near enactment in a New York legislature, serve as publicity springboards even when they fail of enactment. If the so-called dog bill should ever go through the Congress in a preadjournment legislative jam the event would be a catastrophe. Although these bills in the Congress apply only to the District of Columbia, they would serve, if passed, as patterns to be copied in state legislatures.

"In addition to attempting to effect state and national legislation, the antivivisectionists, by creating uproar and emotional tension, have succeeded in diverting many stray dogs which used to be delivered to medical schools to the gas chamber at the dog pound, thus increasing the difficulties experienced by medical schools in procuring dogs for study. Finally, the antivivisectionists admit that the dog is used as their symbol because of mankind's universal love for dogs. If they once succeed in excluding dogs from use for medical research they will proceed to broaden this ban to include, first, cats, and gradually other animals.

"*The Saturday Evening Post* has done an important and significant service to the health of the American people in exposing the threat of antivivisectionism."

In the **J.A.M.A.**'s "QUERIES AND MINOR NOTES"...

an authority lists eight specifications for a preparation to use in the nose:

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SECONDARY INFECTIONS MAY OCCUR IN ANTIBIOTIC THERAPY

Secondary infections, which are an important aspect of treatment with antibiotic drugs, may result from upsetting the natural balance of microbes in the throat and respiratory system, say two New York physicians.

Writing in a recent issue of *The Journal of the American Medical Association*, Emanuel Appelbaum, M.D., and William A. Leff, M.D., of the Fourth Medical (New York University) Division, Bellevue Hospital, New York City, describe two patients treated with penicillin for pneumonia.

Penicillin therapy resulted in improvement of pneumonia symptoms and disappearance of the microbes which caused the disease, but this improvement was followed by the emergence of a secondary infection caused by a different type of microbes. Symptoms of the new infection disappeared when the patients received streptomycin, the physicians report.

It may be of interest to note, they say, that in both cases during the administration of streptomycin the original infection returned, necessitating supplementation with penicillin.

"The mechanism by which the new infection occurs is not clear," they say, "but may be due to a disturbance in the degree of bacterial antagonism which is normally present. It is possible that the removal of bacteria with a specific antibiotic causes insensitive organisms to increase not only in number but also in virulence."



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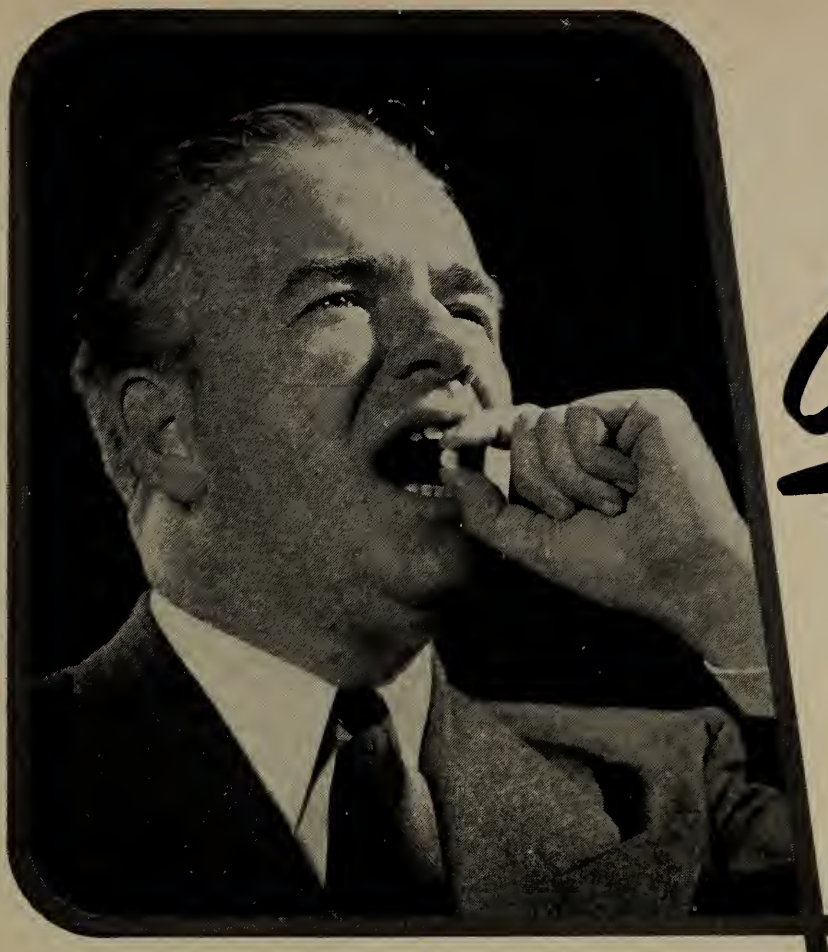
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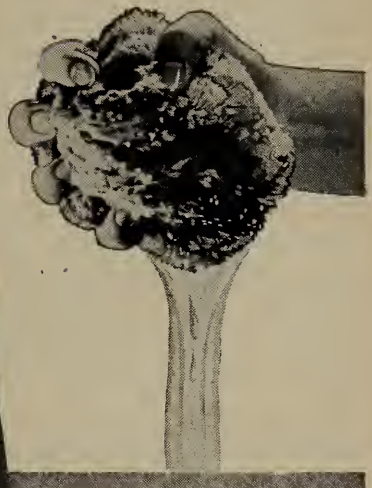
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Aureomycin, the new golden-colored antibiotic drug, is being used to treat patients with Rocky Mountain spotted fever of the eastern type, undulant fever, typhoid fever, and certain infections of the urinary tract, report five researchers from the Department of Preventive Medicine, Johns Hopkins University School of Medicine, Baltimore.

Writing in a recent issue of *The Journal of the American Medical Association*, the researchers—Morton S. Bryer, M.D.; Emanuel B. Schoenbach, M.D.; Caroline A. Chandler, M.D.; Eleanor A. Bliss; and Perrin H. Long, M.D.—report on clinical tests in the treatment of these diseases with aureomycin and on tests with animals to determine the effectiveness of the drug against other diseases.

Aureomycin is one of the newer drugs produced from molds. It is manufactured from the chemicals made by a thread-shaped mold that belongs to the group that produces streptomycin.

Five patients with Rocky Mountain spotted fever of the eastern type who were treated on the third to the fifth day of illness had no fever and showed no symptoms of the disease within 12 to 72 hours.

A patient with chronic undulant fever had no fever three days after aureomycin therapy was begun. Laboratory cultures of the patient's blood, which had been repeatedly positive for the disease, became ster-

(Continued on Page 30)

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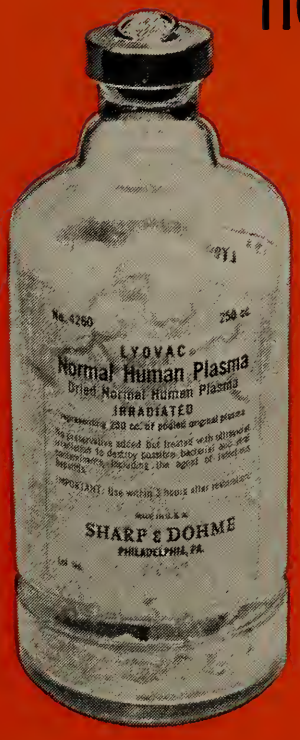
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(Continued from Page 28)

ile 48 hours after treatment with aureomycin was begun. This patient has shown no fever and no symptoms for more than two months, and blood cultures have remained sterile for the same length of time.

Two typhoid fever patients treated with aureomycin showed "favorable initial responses."

Infections of the urinary tract in two patients "were sterilized, and evidence of inflammation disappeared when patients were treated with aureomycin by mouth," the article says.

Aureomycin was administered to patients in the clinical tests by mouth in six doses daily and by injection four times daily. The injections were "tolerated but with signs of moderate local irritation," according to the researchers.

Experiments with animals and the clinical results show that aureomycin prevents the growth of and kills numerous bacteria of different types, they add.

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FIND BLOOD TRANSFUSIONS EFFECTIVE FOR HEMOPHILIA

Blood transfusions are effective in controlling hemophilia over long periods of time, report two researchers from the Medical Research Laboratories, Beth Israel Hospital and the Department of Medicine, Harvard Medical School, Boston.

Hemophilia is an inherited condition in which the blood does not clot readily.

Writing in a recent issue of *The Journal of the American Medical Association*, the researchers—Benjamin Alexander, M.D., and Greta Landwehr, B.S.—say that "observations on patients treated over a period of 10 to 20 months indicate that this approach provides amelioration of the bleeding tendency."

Hemophilia occurs mostly in men, although women "carry" the disease and transmit it to their sons. Slight accidents, which would have little effect on a normal person, may cause fatal hemorrhage in persons with hemophilia.

Four patients with the disease were given blood plasma three to four times weekly by the researchers. The blood transfusions were always followed by a drop to normal or nearly normal in the time required for the patients' blood to clot, says the article. Two of the patients treated who had not been able to take part in active sports played baseball and basketball after receiving blood plasma.

(Continued on Page 44)

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FIND BLOOD TRANSFUSIONS EFFECTIVE FOR HEMOPHILIA

(Continued from Page 42)

Of the 10 reactions which the researchers observed during the study, only four were moderately severe or severe with symptoms of chills, drop in blood pressure, and headache. This incidence of reactions was only slightly more than 1 per cent, the researchers say. One patient developed jaundice, probably from the transfusions, they believe.

Blood plasma is effective against hemophilia only as long as transfusions continue to be given, and the treatment does not cure the underlying condition of the disease, the article emphasizes. Yet this treatment is the first reported which is effective in controlling hemophilia over a long period of time, the researchers point out.

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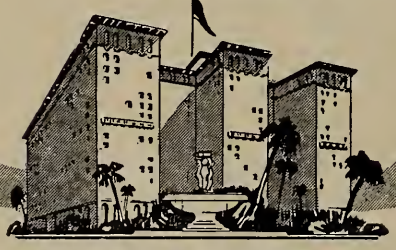
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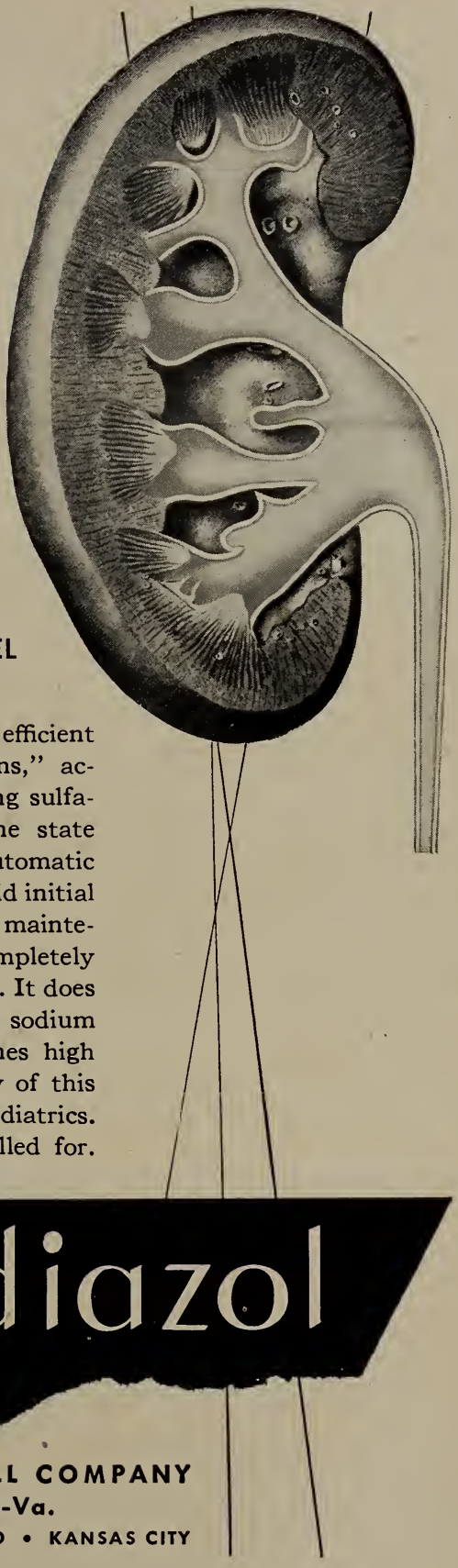
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TUMORS MAY CAUSE HIGH BLOOD PRESSURE

High blood pressure in some persons appears to be caused by a certain type of tumor found in the adrenal and coccygeal glands, along the nerves, and in other organs, says George F. Cahill, M.D., of the J. Bentley Squier Urological Clinic and the Department of Urology, College of Physicians and Surgeons, Columbia University, New York.

Writing in a recent issue of *The Journal of the American Medical Association*, Dr. Cahill points out that this kind of high blood pressure can be cured by locating the tumor with x-ray and removing it by surgery.

Cases which Dr. Cahill has treated show that this type of high blood pressure seems to result from the release of adrenalin from these tumors. It occurs both in children and in adults and is sometimes difficult to distinguish from hyperthyroidism, hysteria, and psychoneurosis, he says. It may be continuous or may occur only in acute attacks, the article points out.

Symptoms consist of a pounding headache, pronounced beating of the heart, constriction of the hands and feet, and pain just above the stomach, according to Dr. Cahill.

Commenting upon Dr. Cahill's article, Dr. Earl E. Ewert of Boston says in the same issue of *The Journal* that persons who appear to have typical seizures of epilepsy may also be suffering from this type of tumor.



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URGE USE OF DOCTOR FACILITIES FOR CANCER DETECTION

The cancer program will be significantly advanced by encouraging full use of existing facilities in the offices of physicians, points out an editorial which appears in a recent issue of *The Journal of the American Medical Association.*

The editorial follows in part:

"The attack on cancer is now enlisting general cooperation. Early detection is imperative and suggests periodic examination of well persons, especially those over 40, and medical examination of persons with symptoms of one of the seven danger signals of cancer. Since there can never be enough 'cancer detection clinics' to handle 142,000,000 persons, the detection program should and must be expanded through the offices of practicing physicians.

"Such examinations in physicians' offices would provide the country with over 100,000 detection centers.

"Theoretically, detection centers could be set up in hospital outpatient departments or in clinic buildings and provide detailed examination. If applied to persons without symptoms (as was the intention) only approximately one cancer was detected in each thousand persons so examined. Applied to persons with symptoms, or to an exclusively elderly female clientele, the percentage yield was much higher. Since it costs approximately $25 per case to do the complete physical examination once recommended, each case of cancer discovered cost about $25,000. Attempts to provide impersonal mass examination clinics will add greatly to the cost of medical care. The actual value of such procedures is still in doubt.

"The creation of additional diagnostic facilities is frequently urged. For over 25 years prior to 1941 the Veterans Administration had unlimited diagnostic facilities, yet the diagnostic work performed at most veterans hospitals during that period was not accepted as reliable by most physicians. In other words, 'facilities' without interested, alert physicians mean little or nothing.

"Every practicing physician should emphasize the need for and the importance of annual physical examination of persons past 40. Approximately 45 per cent of cancer in women involves tissues or organs readily accessible to relatively simple examination. In men the corresponding figure is only 14 per cent."

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INSOMNIA SUFFERERS NEED EDUCATION ON SLEEP

Chronic sufferers from insomnia which has no physical cause can obtain relief by changing their ideas about sleep, says Herman M. Jahr, M.D., associate professor of pediatrics at the University of Nebraska College of Medicine and editor of the Nebraska State Medical Journal.

Writing in a recent issue of *Hygeia*, health magazine of the American Medical Association, Dr. Jahr says that "most of these people have so many erroneous notions of what they call insomnia that it becomes an obsession and keeps them awake."

Although sleep is a necessity, how much and over what intervals each person should sleep varies. Sleep is guided by habit and convention, for many night workers apparently learn to sleep as well in the daytime as other persons do at night, the article indicates. What is restful sleep to one person may be considered restless by another, according to Dr. Jahr. Scientists have not yet devised a way to estimate the amount of sleep an individual needs, he observes.

Poor sleepers fall into four groups—those who have difficulty in falling asleep, those who sleep fitfully and whose sleep is interrupted, those who wake up early, and those whose insomnia is a combination of all three—the article says.

"In the first group we find the tense, stubborn, aggressive individual who takes himself and his mission on earth far too seriously for his own good and for the good of his family, his friends, and his business associates. He no sooner retires than he begins to fidget and squirm. With each turn his anxiety over not sleeping increases. Reading increases his irritation because he is too weary to concentrate. The question 'Why can't I sleep?' is uppermost in his mind. He ends up fighting sleep instead of relaxing and going to sleep. Ultimately, however, fatigue gets the better of him and he falls asleep in spite of himself.

"In the second category is the middle-aged sufferer who frequently goes to sleep soon after retiring but awakens some time during the night with a muscle cramp—not an uncommon occurrence for a man of his age—a feeling of fullness in the chest, or heartburn. His heartburn may be due to overeating or to heart disease, cancer, ulcers, or a good many other conditions which may, but seldom do, account for his symptoms. He proceeds to take mental inventory of his earthly possessions and wonders about provisions for the future of his family. He spends hours tossing around in anxiety worrying about why he cannot sleep.

"In the third group is the elderly person whose activities have become restricted. He takes frequent catnaps during the day and because of a greater tendency to fatigue as well as a reduction in general interest, retires early. He may complain of poor sleep, but in reality he is only an early riser. He usually gets more sleep than the average younger person who retires late and gets up at the accustomed hour in the morning."

Here are Dr. Jahr's suggestions to all types of sufferers from insomnia:

(Continued on Page 52)

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(Continued from Page 50)

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2. Cultivate an agreeable philosophy of life. Don't take your worries to bed. If you must worry, remember that you will be able to worry better after you have had a good night's sleep.

3. If you are hungry just before retiring, eat. If coffee and a "night-cap" make you tense or keep you awake, avoid them. If you are middle-aged, avoid smoking excessively. If you turn in your sleep, remember that frequent turning is necessary to keep the muscles from getting "bound."

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JOURNAL SAYS EWING HEALTH PLAN WOULD NOT SATISFY AMERICANS

In its first reply to Oscar Ewing's 10-year multi-billion dollar health program, including compulsory sickness insurance, the American Medical Association says that "the amount of medical care that is given to most people of the world under their compulsory sickness insurance plans would never satisfy the people of the United States."

An editorial in a recent issue of *The Journal of the American Medical Association* says that the federal security administrator's health figures are "the same old figures that the proponents of government medicine have been launching at periodic intervals for the last 20 or 30 years."

The editorial says:

The National Health Assembly apparently has culminated in a book called "The Nation's Health: A Ten-Year Program." Anyone can buy this work for $1 from the Superintendent of Documents in Washington. As anyone with any knowledge of what goes on could have predicted, the report is devoted largely to arguments in support of a government health insurance program, their principal arguments being an attempt to indicate the parlous state of the health of the American people. The answers to the nation's health problem developed by the Ewing report include, first, more doctors, dentists, nurses and other auxiliary medical personnel; second, the addition of 600,000 hospital beds by 1960, and, third, a nationwide compulsory sickness insurance plan. Here are the same old figures that the proponents of government medicine have been launching at periodic intervals for the last twenty or thirty years. Some of them are requoted in a Washington Letter in this issue of *The Journal.* These undocumented statistics would be ignored if they were not being used in such a desperate, final gasp by the Federal Security Agency.

In an interview to the press on September 2, President Truman supported the Ewing program, saying that he is compelled to advocate national health insurance because he sees no other possible way of bringing medical service to fully half the American people. Just how hard have President Truman and Oscar Ewing tried to see some other way? Just whom have they called upon to help them look?

Recently the general assembly of the World Medical Association met in Geneva with a considerable number of nations of the world represented. Had Mr. Ewing or President Truman been present—or even been represented by someone capable of evaluating the opinion of the physicians of the world about what compulsory sickness insurance has been doing to medical practice in other countries—they would be perhaps a little less certain on the point that compulsory sickness insurance is the answer to difficulties in securing medical care. The amount of medical care that is given to most people of the world under their compulsory sickness insurance plans would never satisfy the people of the United States. The inevitable faults of these systems, which have been emphasized to the American physicians and to the American people for a good many years, are now coming vividly to light. Great Britain embarked on

(Continued on Page 58)

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JOURNAL SAYS EWING HEALTH PLAN WOULD NOT SATISFY AMERICANS

(Continued from Page 56)

its new National Health Act on July 5. People in England may now go to the doctor without calculating the cost of the service. They may be supplied with spectacles and teeth without additional costs. They may have consultants and beds in hospitals without reference to individual payments for services rendered. That is what the National Health Act of Great Britain promised them. Do you think that they get it? No, indeed! They queue up to see the doctors formerly they could have seen by appointment. The doctors write formulas and prescriptions and reports many hours in advance of the time when they see the patients because otherwise they would never have time to see the patients. Many a physician is already satisfied that he cannot work under the Act. The unfortunate public have no way of knowing whether or not what they get is good medical service or something to make them think that they are being given attention. The greatest folly in the world is the manner in which Great Britain embarked on a nationwide health service without hospitals, doctors, nurses, drugs or money to supply what they promised, and an even greater folly would be the attempt to offer a similar service in the United States and to gulp the entire medical problem of the nation in a single swallow.

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California MEDICINE

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Heart Failure of Pulmonary Origin

JOHN MCMICHAEL, M.D., *F.R.C.P. Edinburgh, F.R.C.P. London*

BEFORE considering right heart failure consequent upon disturbances in the lung circulation, it is well to be reminded that the commonest cause of right heart failure is left heart failure. Bloomfield, Cournand and their co-workers (1946) have, in fact, demonstrated that the pressure in the pulmonary artery in mitral stenosis may rise to over 100 mm. mercury, a level well above that which occurs in cases of emphysema. In differential diagnosis some of the common congenital faults such as interatrial septal defect and pulmonary or subpulmonary stenosis have to be kept in mind. We have seen very complex conditions arise when such congenital defects have become complicated by acquired severe lung disease.

A useful working classification of the causes of pulmonary heart disease is given in the table. In pathogenesis there are two main factors:

1. *The obstructive factor.* This is most clearly exemplified by massive pulmonary emboli, which pack the branches of the pulmonary artery, producing a gross reduction in blood flow, and an acute, often disastrous, state of collapse. Less massive, but oft-repeated embolization from tumors or recurrent thrombosis of leg veins may produce a clinical picture which is less dramatic; slowly progressive breathlessness with evidence of right heart enlargement are then the main signs. In certain places in the tropics where schistosoma infections are important, the ova may get into the systemic circulation and block the lung vessels. Although right heart hypertrophy and pulmonary artery enlargement are common, death from consequent heart failure is surprisingly unusual.

2. *Pulmonary anoxia.* Motley and others (1947) and also von Euler and Liljestrand (1946) have shown that a reduced oxygen tension in the lungs will raise the pulmonary artery pressure very considerably. It seems likely that this mechanism may contribute in such conditions as kyphoscoliosis. It is well recognized that pulmonary ventilation becomes seriously impaired in patients with gross deformity of the thorax, and patients frequently die with signs of right heart enlargement and failure. Examination of the lungs in such patients reveals no anatomical causes of vascular obstruction, and there are many instances in which there is no bronchitic element. It is clear that some functional disturbance must be postulated and the arteriolar constrictive reaction to low oxygen tension may be a clue. In the anoxic group of pulmonary heart disease, the arterial blood oxygen saturation is found to be reduced from the normal 95 per cent to below 80 per cent. This reduction of available arterial oxygen brings in a further cardiovascular reaction similar to that in anemia: the cardiac output is often increased above the resting level, and this constitutes a further load on the heart.

Very frequently the factors of vascular obstruction and anoxia are mixed. In silicosis one may see a type

TABLE 1.—*Classification of the Causes of Pulmonary Heart Disease*

1. ACUTE: Massive pulmonary embolism.
2. SUBACUTE: (a) Lymphatic miliary carcinomatosis.
 (b) Embolic carcinomatosis.
3. CHRONIC: A. *Lung Disease.*
 (a) Emphysema heart disease, due to
 (i) Bronchitis
 (ii) Bronchiectasis
 (iii) Cystic disease
 (b) Fibroid lung, due to
 (i) Tuberculosis
 (ii) Sarcoidosis
 (iii) Scleroderma
 (c) Pneumoconiosis, due to
 (i) Silicosis
 (ii) Anthracosilicosis.
 B. *Vascular Disorders of the Lungs.*
 (a) Primary pulmonary hypertension
 (b) Recurrent pulmonary embolism
 (c) Schistosomiasis.
 C. *Kyphoscoliosis.*

Presented October 28 before the Nineteenth Annual Postgraduate Symposium on Heart Disease of the Heart Division of the San Francisco Tuberculosis Association, and November 5 before the Eighteenth Annual Postgraduate Symposium on Heart Disease of the Los Angeles Heart Association.

of endarteritis in the vessels which is present along with gross lesions which probably impair pulmonary ventilation. The work of Hickam and Cargill (1947) has shown an apparent rigidity of the pulmonary vascular bed in emphysema.

CLINICAL MANIFESTATIONS

1. *Acute cor pulmonale.* Packed pulmonary emboli commonly complicate severe medical or surgical illness. With or without warning symptoms of small peripheral pulmonary emboli, the patient suddenly develops circulatory collapse with a feeling of air hunger and substernal oppression. The venous pressure is raised in the neck veins, while the circulation is severely reduced with accompanying pallor, sweating, pulse of small volume and reduced blood pressure. The veins in the neck are engorged, but careful inspection in the early stages may be necessary to perceive this sign. Exaggerated pulsation over the right ventricle and possibly a gallop rhythm may be noted. The electrocardiogram will reveal evidence of acute right ventricular strain and even the acute development of a right bundle-branch block pattern.

Practically the only other acute vascular collapse which may simulate this condition results from rupture of the aorta into the pericardium. Here, also, we encounter peripheral collapse with a raised venous pressure.

2. *Emphysema heart.* This condition, in our experience, is by far the commonest variety of pulmonary heart failure. Most of the patients are over 40 years of age, and there is a considerable preponderance of males, in my experience nine to two. The breathless bronchitic, whose dyspnea persists between attacks, has advanced to a stage at which emphysema is sufficiently pronounced to interfere with the normal oxygenation of his blood. Attacks of giddiness and fainting commonly occur at this stage.

Sooner or later evidence of right heart hypertrophy, and then failure with congestion and edema, will complete the picture. The patient is dusky blue, and his veins are congested; but in contrast to the patient with low output heart failure, whose extremities tend to be cold and blue, the hands, nose and ears are usually warm. The pulse is rapid (90-120) and is of good volume, as might be expected from the slightly raised cardiac output. A curious and interesting feature is the occasional presence of papilledema and retinal hemorrhages. Complicating exacerbations of bronchitis are often present and seem to be precipitating factors in determining failure. When there is accompanying asthma or bronchiolitis the patient is orthopneic, but in some striking cases, without associated bronchial obstruction, he may be most comfortable in a completely recumbent position, even though venous engorgement is gross. Terminally hydrothorax and edema may develop at the lung bases, a mechanical explanation of which is not easy to conceive. The cardiac output is usually falling at this stage and a general cardiac failure of a maloxygenated heart may be part of the terminal picture.

Apart from evidence of right hypertrophy, which may be difficult to detect clinically as the heart is often concealed by enlarged lungs, there is little to be made out on physical examination of the heart. Triple rhythm may sometimes be audible to the left of the sternum. A diastolic murmur of pulmonary insufficiency is rare. Radiologically, enlargement of the pulmonary artery is common, but it is only occasionally that right ventricular hypertrophy can be recognized with certainty in the roentgenogram. The electrocardiogram shows evidence of right ventricular preponderance, and this is often present before the other signs of right heart failure develop. Auricular fibrillation, an almost constant accompaniment of failure in mitral stenosis, is exceptional in emphysema heart, occurring in only about one case in ten.

The arm-tongue circulation time is normal. Polycythemia is unusual, but it does occur sometimes. It is perhaps worth noting that the arterial oxygen reduction may be much greater in severe congenital heart disease than in emphysema, and the bronchial infection in the latter condition may possibly interfere with bone marrow activity. Blood alkali reserve is often raised and plasma chloride correspondingly reduced.

3. *Acute circulatory failure from sudden reduction of negative intrathoracic pressure.* Patients with emphysema who develop a superadded pneumothorax of the valvular variety, or who have a large bulla which may blow up in a similar manner, are likely to become acutely distressed with severe dyspnea, gross air-hunger, and a pulse of poor volume and low pressure. In one such emphysematous patient who had pneumothorax the intrathoracic pressure fluctuated around zero, while the hydrostatic pressure in the right auricle remained extremely low. Filling of the heart, which normally takes place at an effective filling pressure of 7 cm. water (2 cm. hydrostatic pressure plus 5 cm. negative intrathoracic pressure) was grossly interfered with, and the cardiac output was 2.4 liters per minute (normal 5.3). In spite of the low output in this particular patient there was electrocardiographic and clinical evidence of right heart hypertrophy, showing that the raised pulmonary resistance is independent of the high cardiac output factor. This is a variety of acute circulatory failure which of course is easy to differentiate from chronic cor pulmonale with venous congestion.

4. *Other clinical varieties.* Patients with right heart failure must be subjected to detailed study if the causal factors are to be completely comprehended. Sometimes these may be obvious on radiological examination of the chest. Silicosis, tuberculosis. or non-tuberculous fibroid lung may be recognized. Among the rarer causes are the following:

Sclerodactyly. In this condition, the skin over the fingers becomes thickened and this is associated, in the early stages, with undue coldness and blanching on exposure to cold (Raynaud phenomenon). Along with this, there are other features such as rarefaction of the terminal phalanges, subcutaneous calcinosis, pigmentation of the skin, and visceral affections of the esophagus, lungs and heart. A diffuse fibrous change affects the walls of the alveoli; right ventricular preponderance and breathlessness may develop.

Recurrent pulmonary embolism was first recognized by Ljungdahl (1928) and my own experience would confirm this as a clear entity. Progressive dyspnea and pain over the liver are the major symptoms. It is noteworthy that the patients may have little pleural pain and no hemoptysis. Electrocardiograms show evidence of right ventricular hypertrophy together with distention of the pulmonary arteries. Pathologic changes consist of gross hypertrophy of the right ventricle with recent as well as old organized and recanalized emboli in the lung arteries.

Secondary carcinoma in the lungs. A widespread dissemination of secondary cancer may take place through the bloodstreams or along the peribronchial lymphatics. These modes of spread may affect the lungs in different ways; tumor cells within the lung vessels may be associated with surrounding thrombosis and organization. Lymphangitis carcinomatosa may be associated with obliterative endarteritis as a result of invasion of the vessel walls by growth. In these instances the right heart stress results from obstruction of the lung vessels. A suffocating form, however, occurs as distinct from the vascular obstructive variety, and this may, of course, lead to the anoxic type of pulmonary heart failure. In these cases the cancer is usually of a scirrhous type with contraction of scar tissue around the bronchioles and perhaps even invasion of the bronchial lumen by growth. In such instances the raised venous pressure is accompanied by rapid circulation, warm hands and a full bounding pulse.

Primary pulmonary hypertension. There are now in the literature many instances of failure of the right ventricle with associated pulmonary vascular sclerosis, usually described as cases of primary pulmonary hypertension. The sclerosis in these cases affects the small arteries of the lungs, which are usually spared in mitral stenosis. The diagnosis rests on the exclusion of other causes of pulmonary artery enlargement. By means of right heart catheterization the pressure in the right ventricle is found to be greatly raised, and the pulmonary arterial pressure itself, when measured, is raised to figures like 80-100 mm. mercury. Postmortem studies on such patients are often somewhat obscured by the coincidence of numerous pulmonary emboli, which complicate this and all other varieties of terminal heart failure with such great frequency.

Treatment. As in most other diseases the key to good treatment is the recognition of the cause, and an understanding of the underlying mechanisms. In the obstructive variety due to packed pulmonary embolism the essential therapeutic measure is the prevention of further leg vein thrombosis and consequent embolization of the lungs. Anticoagulant remedies such as heparin by injection, and dicumarol by mouth, with proper attention to control of coagulation times, are indicated. The high venous pressure is probably part of the mechanism maintaining blood flow from the right heart through the lungs, and its reduction by venesection or digoxin is undesirable. Patients should be kept quiet with morphine, and if no further embolization takes place, excellent and complete recovery, with restoration of electrocardiographic changes to normal, can take place in a few weeks.

In the anoxic form, best exemplified by emphysema, it is important to keep in mind that the high venous pressure is probably also a compensatory phenomenon maintaining the necessarily raised cardiac output. Venesection and digoxin may do harm; the inefficacy of digitalis preparations in pulmonary heart disease was recognized by Vaquez (1928) as a result of many years of astute observation of clinical results. He recognized that strophanthin preparations, particularly ouabain, might have some beneficial action in these patients, and we now have a good deal of experimental evidence in support of that observation.

The most successful measure in treatment, however, is use of an oxygen tent. By raising the arterial oxygen saturation, the excessive strains on the right ventricle seem to be lifted. If the patients are kept in a tent, for weeks if need be, one may see the most dramatic recoveries in conditions which at first appear almost hopeless. If the patient can be kept alive until the causal exacerbations of bronchitis have subsided the asphyxial condition becomes more and more easy to relieve. If there are any potent remedies for the superadded bronchial infection, they should be used. Our own experience, however, has been disappointing in this respect. Penicillin inhalations simply alter the bacterial content of the sputum without notably shortening the illness.

The right heart tolerates an overload less easily than the left. This has been shown experimentally by Müller (1937) and it may have something to do with the fact that an increased aortic pressure load on the left ventricle automatically increases the blood supply to the heart through the coronary arteries which take origin from the base of the aorta. No such automatic increase takes place when the right heart is subjected to pulmonary hypertension. Patients with pulmonary heart disease, therefore, are always in a precarious condition and, if the disease is one of the chronic forms, they do not readily tolerate more than one or two attacks of failure.

Postgraduate Medical School of London.

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CAUSALGIA

A Review

EUGENE M. WEBB, M.D., *San Francisco,* and E. W. DAVIS, M.D., *Portland, Ore.*

"Causalgia defies every therapeutic method with an obstinacy that drives one to despair."—TINEL.

PERCIVAL POTT mentioned "certain painful afflictions of the nerves" in connection with injuries of the extremities, but it was not until 1813 when Alexander Denmark[9] reported a case that causalgia was clearly described. The patient, a soldier, had been struck by a musket ball just above the inner condyle of the humerus with a resulting radial nerve palsy. Denmark described the intense burning pain, the prostration, the trophic changes, the loss of function and even a tender nodule at the site of the wound. He believed that relief might follow section of the nerve above the level of the lesion, but at the insistence of the patient and with the advice of his colleagues the arm was amputated. Complete relief was reported. Denmark's dissection revealed a lacerated but not divided nerve, intrinsic and extrinsic scar, as well as a tiny fragment of lead embedded in the nerve.

In 1864 James Paget[34] gave a brief, clear and forceful account of the disorder which was cited by Wier Mitchell[31] in his more generally recognized and more complete report later in the same year. Mitchell's description is widely hailed as a classic and even today is extensively quoted, often with an appended comment that nothing has been added to the description since. While the general truth of such homage is not to be denied, the force and lucidity of Mitchell's description at times outstrip the absolute accuracy of his observation. One may attempt, therefore, to replace the traditional introduction to the nosography of causalgia with a summary of those factors which have been found to appear repeatedly in the reports of later observers.

Attention should be drawn to the widespread lack of agreement over clinical definition. The terms causalgia, major causalgia, reflex sympathetic dystrophy, thermalgia, synesthesialgia, post-traumatic painful state, painful osteoporosis, Sudeck's atrophy, and the causalgic state are all used with varying degrees of discrimination. Moreover, the so-called minor causalgias may or may not be included in one of these terms. Finally, the minor causalgias are variously defined. Some consider them to be characterized merely by relatively slight involvement and suffering; others reserve the term for more or less well defined clinical entities such as Sudeck's atrophy or post-traumatic osteoporosis. De Takats[44] calls for a redefinition, stating that frank causalgia is readily recognized but that there are a variety of related afflictions dependent upon the same neural mechanisms which are readily and commonly misunderstood. Evans[11,12] considers that causalgia is a misnomer, as does Stoppford,[43] and states that burning pain may or may not be present. Homans[18] suggests that true causalgia is seen only in injuries to major nerves and that other similar disorders which are usually due to relatively minor injuries be grouped together under the term "minor causalgia." Insofar as possible this classification will be followed in this presentation.

On the major clinical features all authors are in agreement. These include burning pain, trophic changes, failure of the pain to remain within the bounds of the distribution of the affected nerve, profound physical and psychical deterioration, the tendency to paroxysms of pain and to aggravation of pain by emotional stimuli. Today many would also include instant, if but temporary, relief following sympathetic block in the list of essential diagnostic criteria. The Medical Research Council in 1920 set up the following as the essential characteristics of causalgic pain: (1) spontaneous; (2) hot and burning, intense, diffuse, persistent, but subject to exacerbations; (3) excited by stimulation which does not necessarily produce a physical effect on the limb; (4) aggravated by emotional excitement which usually brings on a paroxysm. Mayfield[29] (1947) states that the diagnosis can always be made when there is (1) burning pain associated with trophic and vasomotor changes in an extremity following a peripheral nerve injury; (2) aggravation of the pain by emotional stimuli; and (3) instant relief following sympathetic block.

On other points there is less agreement. Mitchell[32] reported the disorder as being present in 19 of 50 peripheral nerve injuries which came under his observation. At the other extreme, Carter[8] in an excellent and thoughtful paper (1922) reported true major causalgia present in only four of 3,000 peripheral nerve injuries. In an attempt to establish a reasonable figure for the overall incidence, figures have been combined from eight reports that give evidence of accuracy and freedom from obvious sampling errors. Neither Mitchell's nor Carter's figures are used. From these papers there were culled 140 cases of *major* causalgia occurring among 3,326 cases of peripheral nerve injury, an incidence of 2.1 per cent.

There is a similar lack of agreement as to the distribution of causalgia through the various major nerves. The earlier authors, with varying degrees of rigidity, uniformly label causalgia primarily a disease of the median and sciatic nerves. Reports from the most recent war do not entirely support this. Thus, Rasmussen and Freedman[37] in a series of 100 cases report involvement of the median nerve

From the Division of Neurological Surgery, University of California Medical School, San Francisco.

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in 17, multiple nerves in 17, brachial artery and great nerve in 11, brachial plexus in 10, ulnar nerve in 9, radial in 6, and sciatic in 8 cases. Freeman[14] reports that in 91 cases the radial nerve was affected in 18, the median in 15, the ulnar in 13, the brachial plexus in 11, and the sciatic nerve in 5. From about 200 cases reported by five authors composite figures reveal involvement of the median nerve in 25 per cent, the sciatic in 22 per cent, the brachial plexus in 18 per cent, the ulnar nerve in 14 per cent, the radial in 12 per cent, the posterior tibial in 5 per cent, and the peroneal nerve in 3 per cent. These percentages are indicative of the incidence of causalgia in a given nerve in relation to other major nerves, and not of the frequency in relation to all causalgic states. This is the only figure that one can supply that is not subject to the sampling errors of local combat factors, differences in diagnostic criteria and other variations.

Mitchell reported that pain always appeared some time after the nerve injury and innumerable accounts since then have contained the same statement. Leriche[22] denied this and cited a case of causalgia in which the injury occurred in his presence and in which the characteristic burning pain appeared immediately. Rasmussen and Freedman state that 48 of 100 patients had burning pain within six hours, and Ulmer and Mayfield[49] report the typical burning pain as being present from the instant of injury in 44 of 100 cases.

Whether or not causalgia may occur in the presence of a completely severed nerve is likewise unsettled. The preponderance of opinion is that it does not, and many who express such a view are extensively acquainted with the subject. Carter, Leriche, and Ulmer and Mayfield have all found for the negative. However, Allbritten and Maltby[1] report two cases of causalgia, and Bondarchuck[6] reports one more, occurring in the distribution of a completely divided nerve.

The underlying pathological and neural mechanisms have long been a source of controversy and conjecture as well as research. While the remarkable penetrations of Wier Mitchell into the subject are well known, attention may be directed to Létiévant[23] who, though less well known, is no less profound. In an extraordinary monograph which appeared in 1873, Létiévant discussed causalgia and related painful states with rare insight.

He stated that in such conditions there are three anatomical sites fundamental to the mechanism: the peripheral nerve and its point of irritation, the spinal centers, and the sensorium. He stated that theoretically the pathological activity could be interrupted at any of the three sites, but that the only one surgically accessible (in his day) was the peripheral nerve. The steps he listed in the development of the abnormal mechanisms are:

1. Local irritation due to the injury.

2. Transmission of impulses from this site to the spinal centers.

3. Here, in the spinal centers, if the impulses are strong enough and sustained long enough a state of abnormal neural activity appears and spreads to adjacent centers.

4. Having produced this spread, not only do the usual impulses ascend to the sensorium, but other impulses which have arisen in the adjacent disturbed areas ascend, producing an extraordinary amount of painful sensation.

5. The spread to adjacent areas likewise causes the associated peripheral phenomena.

Létiévant states that neurotomy interrupts the irritating impulses and that while the abnormal neural activity may reverberate throughout the neuroaxis for a time, usually this dies out and relief then follows.

In 1916 Leriche[20] proposed that the underlying abnormality is a perversion of sympathetic activity and that treatment therefore should be directed to the modification of the sympathetic system. Later in the same year Meige and Athanassio-Bénisty[30] presented clinical, physiological and histological evidence in support of such a concept. By 1921 at least, Tinel[46,47] had subscribed to the same view.

In 1917 Stoppford[43] reported two constant pathological findings, partial division of the nerve and interstitial fibrosis, findings which have since been shown to be nonspecific.

Carter[8] reviewed the subject and discussed the possible reasons why the median and sciatic nerves were so susceptible to causalgia. These were given as: (1) both supply special peripheral areas rich in sensory endings, (2) both contain large vasomotor components, (3) both have large intrinsic arterial supplies, and (4) both supply a large arterial arch with large numbers of vasomotor fibers. He also discussed the theories then prevalent and in greater or less degree deflated all. These were (1) paralysis of vasoconstrictors, (2) irritation of vasodilators, (3) abnormal reflex activity, (4) sympathetic abnormalities, and (5) alteration of vascular supply to the median or sciatic nerves.

While causalgia and allied states are seen in industrial and private practice, it is most frequently seen in soldiers. Interest waned between wars, and Carter's paper which appeared in 1922 was the last of importance until just before the last war.

However, during this interval an enormous development in neurophysiology prepared the background against which new cases, which were to appear in such numbers, might be viewed. Understanding has progressed along two main lines; broadly, central mechanisms and peripheral mechanisms. Of these, the former is most widely discussed, most heavily called upon and perhaps most articulately and reasonably expressed by Livingston.[24] The other, the peripheral mechanism, with the striking exceptions of a few papers, remains merely a "seat of irritation," an initiating focus which is all too quickly dismissed in the hasty ascent to higher centers. If, in the discussion to follow, we may temporarily defer Livingston and

Doupe, Cullen and Chance, we may more sympathetically attend other views.

Moser[33] in 1943 proposed that the intimate mechanism lies in the continuous excitation of afferent sympathetic paths which set up an irritation in the thalamus such that peripheral stimuli of all kinds are translated into pain which is referred to the affected limb.

De Takats[44] in 1945, calling on Kinnier Wilson, stated that sensory pathways should be regarded as being susceptible to stimulation at all levels. He proposed that the initial lesion affects the first neuron, which may itself initiate vasomotor reflexes that are predominately vasodilator, as shown by Bayliss.[3] If not treated promptly or properly the disturbance will then ascend to the second neuron which he appears to consider as being in the spinal cord. The third neuron he regards as being in the cerebral cortex, and he stated that under the constant barrage from lower centers the cortex might then become the "seat of projected, self-propelled impulses to the periphery."

Zikeyev,[52] in 1946, stated that miraculous cures are not to be expected because the thalamus is implicated in the ultimate neuropathologic process. He feels that there are two factors in the neural structure of causalgia, a persistent irritation at the site of the injury and a dysfunction of the thalamus. He suggested that the essential striking feature of causalgic pain is its thalamic nature as evidenced by its tendency to spread, even to the whole half of the body, the paroxysms, the psychic effect. He employs Pavlov's concept of preserved inhibition, stating that in causalgia the thalamus and related cortical cells lose this preserved inhibition which is normally maintained by rest and the attendant lack of afferent bombardment.

Rusinov,[38] in 1947, reported peculiarities of action currents from the median nerve of a patient with causalgia. Painful irritation produced an electrogram which differed from electrograms of normal subjects in that there were bursts of relatively high voltage spikes occurring in groups. He feels that this alteration is due to intensification of impulses as they pass the point of damage. One is led to the inference that this intensification is the neuropathological basis of the disorder.

To return to Livingston[24] and the physiological background upon which he draws, we may briefly recall the salient points of Lorente de No's[26] 1938 discussion of the internuncial pool concept. Lorente de No stated that the nervous system contains enormous numbers of interlacing paths with numerous opportunities for the conduction of impulses over divergent routes. During activity these paths are functionally segregated into active and inactive groups. The active groups arrange themselves in convergent chains of relatively simple patterns of which there are but two types, the multiple and the closed. He stated that the mechanism of stimulation of neurons is the delivery of impulses at their synapses. The effect of individual impulses is brief, but the continuous arrival of impulses insures constant stimulation. The neuron responds whenever the simultaneous effect of the impulses that arrive within a period of effective summation reaches its threshold.

Fractionation of internuncial paths and failure of "avalanche discharge" depend upon the rigidity of conditions necessary for any neuronal discharge. In order to have effective summation and discharge, a neuron must have a sufficient number of spacially remote synapses which are activated all at once. Cells in the active chain fulfill this requirement; those in the inactive chain remain on the subliminal fringe.

Lorente de No then illustrated how a neuron which originally could have been fired only by the simultaneous appearance of impulses at two of its synapses may continue to fire even when one of the original exciting impulses drops out. This is due to a closed chain circuit which, as part of its activity, partially excites the neuron in question.

With this in mind we may now summarize Livingston's discussion. He proposed that in causalgia a partial lesion of a nerve is followed by a focus of irritation which transmits to the cord a sustained barrage of impulses that serve to upset the normal functioning of the internuncial pool. The path of incoming impulses is so altered by this abnormal activity of the pool that the pattern of excitation, eventually registering in consciousness, is changed. Continued pool activity in time implicates the anterior and lateral horn cells; the changes in muscle and vasomotor activity resulting from this furnish new sources for pain impulses. Finally, as the intensity of this self-sustaining process is increased, other more distant neurons throughout the central nervous system are drawn into the complex. In speaking of the vicious circle concept he recognizes three components: incoming impulses from the periphery, internuncial pool activity, and motor impulses from the lateral and anterior horns. Of these, if any may be said to be more important, it is the internuncial pool.

Porter and Taylor[35] (1945) reported what they termed a "facilitation reflex" and offered it as partial support of Livingston's discussion. Under experimental conditions they showed that reflex motor response to constant minimal induction shocks to a sensory root of a cat is greatly facilitated by other sensory impulses such as heat or cold or even blowing on the fur.

To turn to the concept of a peripheral mechanism, one finds a report by Katz and Schmitt[19] in 1942 showing that under certain experimental conditions action currents in nerve fiber can initiate impulses in an adjacent fiber. In 1944 Granit[16] and co-workers showed that in isolated sections of peripheral nerve in cats impulses traveling in a motor fiber were capable of initiating impulses in adjacent sensory fibers. Employing the term "artificial synapse" they show that the same phenomena are encountered when such a nerve is partially dam-

aged or crushed. They suggested that these facts might well be fundamental to the pathological activity in causalgia.

With this and similar corroboratory evidence in mind, Doupe, Cullen and Chance[10] in 1944 postulated that causalgic pain might well be due to activation of somatic sensory fibers by efferent sympathetic impulses. They pointed out that sympathetic impulses to digital vessels and palmar sweat glands are greatly increased by emotional stress; moreover there is more or less constant activity in sympathetic fibers in response to thermo-regulating needs, postural activity and pilomotor activity. As a result the pain would appear to be spontaneous, yet would be sharply increased with emotional changes or with pain elsewhere or with respiration, all of which are known to increase both the pain in causalgia and efferent sympathetic impulses. Such a mechanism likewise explains the diffuse character of the pain. Also, pain and temperature fibers, being small, might well be particularly susceptible to sympathetic fiber action currents. If this were true it might explain the burning pain. Finally, it affords a clear-cut explanation of the relief of causalgic pain following sympathetic block.

They pointed out that all observations may be explained on this basis, vasomotor and trophic changes being explicable through antidromic stimulation of afferent fibers. The variable time of onset and the tendency for symptoms to fade, they felt, must be explained by the peculiar and intimate structure of the peripheral leak between the sympathetic and sensory fibers.

This seems a striking and stimulating paper, but so are the views of those who champion the internuncial pool as the fundamental mechanism in causalgia. But each concept, it seems, is incomplete. There are clinical observations which each viewpoint neglects to scan. All will agree that there is some unusual dominating neuropathologic mechanism at work which, by virtue of its own unique capacities, forces the causalgic state into existence. The internuncial pool concept is a useful clinical projection of basically sound neurophysiology. Yet why should one man's internuncial pool become pathologically active and another's not? Or is it to be supposed that this pathological activity springs up full blown in those cases which are marked by burning pain from the outset?

Similarly the concept of an essentially peripheral mechanism as presented by Doupe, Cullen and Chance fails to account for those cases which do not respond to sympathectomy. Nor does this theory explain mirror image phenomena nor other types of unusual spread.

It seems that each concept contains that which the other lacks; that each bears powerful support of its own implication. The one great flaw in the internuncial pool concept is its failure to explain adequately the onset—the first, the basic neuropathologic error. Thus, the artificial synapse could provide the unique, though rarely observed, basic abnormality; the internuncial pool could modify this and in certain cases maintain a self-exciting pathological pattern.

We would conceive of the process something like this: One hundred men, normal, healthy, receive wounds damaging their median nerves; ninety-eight display palsy of various degrees but nothing more. But in the remaining two the intimate and so far inscrutable micro-anatomical derangement will be such that abnormal function appears. The insulation, so to speak, has been carried away but the thus bared conducting mechanism retains its power of function; efferent sympathetic impulses induce action currents in adjacent somatic afferent fibers; pain of a distinctive and baffling nature appears; the patient finds that any activity associated with sympathetic discharge increases the pain. The vicious circle is already in force and the clinical picture continues to develop. One of the two may have the sympathetic outflow blocked early and obtain relief. The other may not, and the continuing whirlpool from lateral horn to the periphery to the posterior horns to higher centers to lower centers and back to the lateral horns draws ever more neurons into the vortex. Finally, interruption of peripheral sympathetic efferents is not followed by relief; the closed chain circuits have taken over and the process is self-exciting.

METHODS OF TREATMENT

Treatment has so progressed since Tinel's time that his company is now rarely sought by the misery of despairing surgeons; yet many, in sorrow still recall that:

> *"Diseases desperate grown*
> *By desperate appliance are cured*
> *Or not at all."*

The first treatment was Denmark's amputation. Mitchell employed blisters; Létiévant, neurotomy. Sicard[40] used intraneural injections of 60 per cent alcohol, as did Turco,[48] Dean Lewis[25] and others. Stoppford advocated section and end-to-end suture; Stoffel[42] used what we would call neurolysis. Some successes are reported for all of these methods. Modern methods may be considered to have begun with Leriche who developed periarterial sympathectomy and segmental arteriectomy. Today, as is well known, treatment is almost uniformly sympathectomy by one means or another.[2,5,7,15,17,21,39]

In 1943 White[50,51] reviewed the treatment of causalgia and concluded that neurectomy, posterior rhizotomy and intraneural alcohol were of no value; that excision of a neuroma was worth one trial but no more; that sympathectomy was excellent, and that cordotomy was often very much worth while.

In 1945 Speigel and Milowsky[41] reported nine cases. All the patients received complete but temporary relief from procaine blocks. One was so improved by one block that nothing further was done. One obtained complete relief from alcohol block, and the other seven were completely relieved by preganglionic sympathectomy. Machabeli,[27] in

1945, reported complete relief in 23 of 25 patients by what he terms "fasciculation," which appears to be a neurolysis.

De Takats[44] in 1945 reported on 54 patients treated in keeping with his concepts. Thirty-six were treated with local procaine with relief; he considered these cases examples of first neuron involvement. Twelve were treated with sympathectomy on the assumption that these were examples of the second stage first neuron class; these 12 obtained relief. There were six patients that he considered to be examples of the second or third neuron class who did not respond to sympathectomy or, in two cases, to cordotomy. Of these, one killed himself, two are in asylums and three are morphine addicts.

Mayfield and Devine[28] reported 15 cases in 1945. Five of the patients had neurolyses, three periarterial sympathectomy. None benefited. Twelve had preganglionic sympathectomy; all obtained complete relief.

Mentioned only to be condemned is a 1945 report of cure of a patient with causalgia by psychotherapy. The appended case history will not support the diagnosis of causalgia.

In 1946 Rasmussen and Freedman[37] reported 100 cases. Of 91 who received procaine blocks, 73 obtained complete temporary relief, 16 marked temporary relief and two showed no change. Of the 91, thirteen obtained complete permanent relief from blocks alone, while 32 more obtained moderate permanent relief. Postganglionic procedures were employed in 21 patients with involvement of the upper extremity and 14 of these obtained total relief; but 13 of 14 patients received total relief in the upper extremity after preganglionic procedures. Moreover, four-fifths of the patients with causalgia of the lower extremity retained some pain after lumbar ganglionectomy.

Ulmer and Mayfield[49] in 1946 reported 75 patients. In two cases the nerve was resected and sutured, with cure. Seventy had sympathectomy. Of these, seven were not completely relieved until a second procedure taking more ganglia was carried out; the remaining 63 patients were completely relieved after the first procedure.

Berry[4] and associates studied tetra-ethyl-ammonium bromide in various disorders including causalgia. Without giving much clinical detail, they stated that it is as effective as sympathectomy—temporarily.

Evans[13] reported 57 patients observed in the Lahey Clinic. Twelve had sympathetic blocks only, 11 with satisfactory to complete relief. Twenty-nine had sympathectomy. Eleven had complete relief, 11 more had 50 to 90 per cent relief, but seven were unchanged.

Rasmussen and Alessi[36] reported the use of Rectocaine, a slowly absorbed local anesthetic, in two cases of causalgia. The first patient displayed complete sympathetic paralysis in the expected area for two weeks and complete freedom from pain for the period of the follow-up which was only ten weeks. The other's sympathetic paralysis lasted for three weeks and there was freedom from symptoms for the period of the follow-up.

In 1946 Allbritten and Maltby[1] reported 67 cases. Sympathectomy was carried out in 30 patients, 28 of whom obtained relief reported as good to excellent. The other two experienced no change.

Zikeyev[52] supplied an interesting report of 37 patients in 1946. It is Zikeyev who believes that the thalamus is so thoroughly involved in the neuropathology. Treatment was surgical followed by prolonged narcotic sleep which was continuous with and immediately followed the anesthesia. It was maintained for five to six days by a nostrum, modestly called "sleeping mixture," which contained sodium bromide, chloral hydrate, tinct. valerian, luminal and pantopon. Of the 32 patients so treated, 31 were completely relieved and one moderately so. However, these figures become somewhat less imposing when the operative procedures are reviewed. Eleven had resection and suture of the nerve, 13 had resection and graft, and eight had neurolysis. And it is known that nerve section is followed by relief in a high percentage of cases.

Mayfield[29] reported 105 cases in June, 1947. He now uses procaine block for diagnosis only. He employs the Smithwick preganglionic procedure for the upper extremity and removes the second and third lumbar ganglia for the lower extremity. Of the 105, all but nine were relieved completely by the first procedure. All of the nine were relieved by a second slightly more extensive procedure.

Freeman[14] in July, 1947, reported 114 cases. All responded temporarily to procaine blocks, but only the mildest cases responded to repeated procaine blocks with permanent and complete relief. The first two patients were treated with preganglionic resection, below the third thoracic and rami of the second and third. These were completely relieved, but only for one week. The stellate and the second and third thoracic ganglia were removed in the next four cases. Two patients showed excellent results, in another the result was fair, but in the fourth poor. The next seven had the stellate, second and third thoracic ganglia and the intervening chain removed and the periarterial sympathetics removed from the subclavian artery. All obtained complete relief of pain; two had excellent functional recovery, but in the other five the peripheral soft tissue changes were so great as to preclude good functional recovery. The next ten patients were treated in this manner but very early. All obtained complete relief and eight returned to duty. The next four patients were treated with early peripheral surgical operation followed by repeated procaine blocks, all with excellent results.

SUMMARY

The literature of causalgia is briefly reviewed.

The various theories of possible underlying mechanisms are examined.

The view is advanced that both the theory of peripheral mechanisms proposed by Doupe, Cullen and

Chance and the internuncial pool concept are fundamental to the complete elucidation of the intimate neuropathology of causalgia.

The results of treatment as reported by various authors are summarized.

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The Surgical Significance of Acute Abdominal Pain

J. William Hinton, M.D., *New York*

In reviewing my observations in two of the larger hospitals of New York over a period of 25 years, I have been disturbed by the frequency with which patients suffering from acute abdominal pain are subjected to laparotomy with resulting negative pathologic findings. Even more distressing is the opinion expressed by many surgeons that exploration with negative findings is preferable to unrecognized acute appendicitis which may develop into peritonitis with a fatal termination. We cannot but question this attitude in view of the present minimal mortality rate from acute appendicitis, including cases with abscesses and general peritonitis.

In a review of acute appendicitis on the fourth division of Bellevue Hospital over a 12-year period from 1928 to 1939, inclusive, we[8] found the mortality rate during the first six years, namely, 1928 to 1933, to be 6.3 per cent and from 1934 to 1939, inclusive, 3.4 per cent. The total mortality rate of 677 patients suffering from acute appendicitis was 5.1 per cent. The diagnosis was based entirely on the findings of the pathologist and not on the findings of the operating surgeon. Among these 677 patients there were 474 cases of unruptured acute appendicitis, 67 cases of localized peritonitis, 88 abscesses and 48 cases of general peritonitis. In 75 per cent of the cases the operations were performed by the house staff, and the junior attending staff performed the other 25 per cent. These statistics represent the results before chemotherapy was instituted.

From 1940 to 1947, inclusive, there have been 265 operations for acute appendicitis with the same percentage of peritonitis and abscesses, the resident staff performing nearly all the operations. There have been four deaths, three of which were caused by cardiac insufficiency. This is a mortality of 1.5 per cent, which eliminates the great fear of death from acute appendicitis. Reasons for the diminished mortality rate include the use of chemotherapy, the more frequent use of plasma and blood and keeping the patient well hydrated at all times. Improved anesthesia and a more careful follow-up by a better trained resident staff are important advances.

Dr. Edgar Burke, surgical director of the Jersey City Medical Center, has been kind enough to allow me to quote his statistics on acute appendicitis for 1947 which include those cases with general peritonitis, local peritonitis, and abscess. The total number of patients operated upon during the year 1947 was 271, with one death or a mortality of 0.36 per cent. These figures are most impressive when one considers that the resident staff performed nearly all the operations.

In attempting to analyze the reasons for frequency of the mistaken diagnosis of acute appendicitis in acute abdominal pain, we naturally attribute most of these errors to the lack of clinical experience of younger surgeons. From my observations I have found this to be true. However, I feel that an additional factor is the basic training of the young surgeon while serving his residency. If he is taught that exploratory laparotomy is indicated in most cases of acute abdominal pain, then such will be his practice.

During the past eight years I have served on the committee on applicants of the American College of Surgeons for New York City. In this capacity I have had opportunity to note that many young surgeons when interviewed present a list of operations done during the preceding year which includes a percentage of appendectomies out of all proportion to the total number of operations. For instance, a surgeon applying for a fellowship in general surgery may present a list of 60 to 100 operations, of which 25 to 35 per cent are for acute or chronic appendicitis. The members of the committee feel that the candidate's percentage of appendectomies is probably four to five times greater than that of the members of the committee.

The teaching of three to four decades ago was to impress upon the clinician that acute abdominal pain represented an acute pathologic process which usually necessitates a laparotomy. We were told that the appendix was the most frequently diseased organ we had to fear. This teaching has become so thoroughly implanted in the mind of the surgeon, and to a great extent in the mind of the internist, that a patient suffering from acute abdominal pain is usually regarded as a candidate for laparotomy. Frequently the operation reveals negative findings.

Certainly a patient with acute abdominal pain should not be rushed into a laparotomy unless there are clear-cut indications that a real pathologic process is present.

Acute abdominal pain may be attributed to three causes.

1. Anxiety neurosis with conversion symptoms or other psychogenic factors.
2. Physiologic conditions, such as painful ovulation, more frequently referred to as intermenstrual or Mittelschmerz's disease.
3. True organic diseases which require surgical care.

It is the first two groups I wish to discuss first, in order to emphasize their importance in making differential diagnosis of acute abdominal pain which may necessitate a laparotomy.

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Conversion symptoms, the emotional or psychogenic cause of abdominal pain, are the type most frequently overlooked. This is apparently due to the fact that most surgeons have been taught that any acute abdominal pain represents true organic disease and therefore necessitates laparotomy. This teaching is not only erroneous, but tragic for the patient who submits to laparotomy because of psychosomatic symptoms. The question is asked: Can true pain exist without some underlying disease condition? Miller[6] states, "May I suggest humbly that pain is what the patient thinks it is and the only clue we have as to whether the patient feels the pain is what the patient says about it."

Bennett and Semrod[1] reported that among 100 patients with psychoneurosis admitted to a university hospital, organic disease, including gastro-intestinal disease, hyperthyroidism, organic cerebral disease, and other diseases of vital importance was diagnosed in 72. One hundred and seventy-nine operations had been performed, at least one-half of them unnecessary. Of these 100 patients, 70 showed satisfactory and lasting improvement under psychotherapeutic treatment. Bennett[2] more recently reviewed the histories of 121 women on whom 205 operations had been performed: 159 major, 84 pelvic, 40 appendectomies, 11 gallbladder, 16 thyroid, 5 postoperative adhesions, 3 kidney operations, 46 minor operations. 12 rectals, 24 on tonsils and nasal sinuses, and one for varicose veins. He stated that it was hard to determine how many of these operations were necessary but in the majority of cases the patient agreed to the operation with the understanding that it would bring relief from nervousness, although the chances are that none of the operations were indicated from that point of view.

The fact that so many patients presenting pain due to psychogenic causes are subjected to unnecessary operations reflects on the teaching, either in medical school or during a residency. Apparently too much emphasis is placed on diagnostic laboratory procedures and too little on clinical evaluation of the history. I am not a psychiatrist and have never had psychiatric training, but I feel that most of us can suspect the presence of a functional disorder merely by allowing the patient to talk and get his history as he presents it without interruption. The history is one means by which psychogenic pain may be suspected and then confirmed or ruled out by a psychiatric consultation.

A number of years ago a physician with whom I was discussing the end results of operations on patients with poor psychiatric backgrounds told me the following incident: A well known surgeon had consented to perform a laparotomy on a patient because she insisted she had a frog in her stomach. At first he tried to dissuade her, but finally he decided to perform the laparotomy and present her with a frog. This was done and the patient was asymptomatic for six months. She then returned and demanded a second laparotomy because of the fact that frog's eggs had been left in her stomach at the time of the original operation. I do not have a further follow-up on this patient, but I do not believe we have to stretch our imagination to guess the end results of such a procedure.

Greenacre reports[3] the following case:

"The patient was seen in the psychiatric out-patient department of the New York Hospital over an 18-month period. She is representative of a group of cases with which we, in a psychiatric clinic of a general hospital, became quite familiar, and I am quite sure it is a group which the medical and surgical physicians also encounter, for patients of this general type come to them first. The patient, a woman of 54, came to us in 1937 with a complaint of pain in the ethmoid region for three years, stomach trouble for ten years, pain across the lower abdomen for two years, and transient sensations of a dead feeling over the back of the head and chest following periods of emotional upset for two years. I am quoting from the patient's own statement of her difficulty and it is noted that her symptoms are all in somatic terms and betray some degree of medical sophistication. She had, in fact, been referred from the medical clinic where she had been considered as predominantly a case of hypochondriasis and this diagnosis seemed borne out by her examination in seven other clinics as well. The number of examinations necessary to arrive at this diagnosis is really impressive.

"Her hospital experience began 32 years ago, when at the age of 22, she had first a dilatation and curettage. This was followed at 24 by a uterine suspension, at 30 there was a right kidney suspension and an appendectomy and later in the same year an ovariectomy, hemorrhoidectomy and another dilatation and curettage at 39. There was a new operative bout, and another suspension of the right kidney and in the same year an operation on the nasal septum. At 40, a complete hysterectomy was followed by peritonitis. At 41-42 a tonsillectomy was done and next a bilateral antratomy which had to be repeated on the right side. At 49, the right kidney was removed and at 52, finally an ethmoidectomy was accomplished. When one looks over this table of operations, it is apparent that they have occurred in general, at four periods in the patient's life; the first at 22-24, the second 30-31, the third 39-40, and the fourth at 49-52. Thus, curiously enough, we note that roughly the patient enters each decade of her life with a surgical initiation; and that the operative work has, as it were, extended itself from below upward, beginning with the genito-urinary system, making a detour into the gastro-intestinal system and finally coming to rest in the naso-pharynx.

"Neither can we now, from behind the screen of these 16 to 17 operations to the lapse of so many years, say much as to the positive indications for the various procedures undertaken. The patient now makes the impression of a morbid willingness to submit to any operative procedure, in the hope of a miraculous relief, which is contrary certainly to all the experience which she has gathered in the past 30-35 years. In other words she now shows an attitude of addiction to surgery, somewhat similar to other forms of addiction."

Wearn[9] in his chairman's address before the Section of Internal Medicine of the American Medical Association in 1947 stated: "Of some 15,000,000 men examined by Selective Service, 1,875,000 were rejected on the ground of neuropsychiatric disorders. This represents 37 per cent of the men rejected for all causes; and even after this initial

screening, 39 per cent of all medical discharges from the army between January, 1942, and December, 1945, were classified as psychoneurosis. At least 5 out of every 10 patients who consult physicians today prove through examination to have no organic basis for their complaints."

Acute abdominal pain is frequently caused by painful ovulation which is not recognized by the surgeon or by the attending physician. It usually occurs in the younger woman in the twenties or early thirties. This condition is also known as intermenstrual pain or Mittelschmerz's disease. A characteristic point in the history is that the pain occurs 10 to 12 days preceding menstruation. There may also be evidence of scant vaginal bleeding at that time.

This condition has been known for over a century, as Pouchet in 1847 discussed it in a book on ovulation and conception in mammals. Sir William Priestly in 1782, Howard Kelly of the United States, and Mittelschmerz in Germany discussed the condition frequently. The diagnosis should not be difficult if we keep the possibility in mind and elicit a careful history. Many a patient will volunteer the information that the pain occurs 10-12 days preceding menstruation and occurs with great regularity. There are no constant pathologic findings in intermenstrual pain either microscopically or macroscopically. There is no unusual thickening of the ovarian capsule which has been suggested as a possible cause of pain. The physiologic nature of the disorder does not interfere with reproduction and is never a cause of sterility. The pain is not of a permanent nature, and in many cases may disappear without any form of treatment.

There is real danger of abdominal hemorrhage resulting from a ruptured graafian follicle or corpus luteum cyst. The hemorrhage may be quite profuse in the peritoneal cavity and in its presence there may be difficulty in ruling out ruptured ectopic pregnancy, a diagnosis that is frequently made by error. A laparotomy is indicated in severe hemorrhage from a ruptured cyst as well as in a ruptured ectopic pregnancy. Sackett[7] has reviewed the subject of intraperitoneal hemorrhage of the ovarian origin and his bibliography is most exhaustive on this type of hemorrhage. In the majority of hemorrhages from a graafian follicle or corpus luteum cyst there is no free bleeding in the peritoneal cavity; if present, it is minimal in amount. The pain is caused by distention of the follicle or cyst.

The treatment of intermenstrual pain is to avoid a laparotomy in the absence of profuse bleeding in the peritoneal cavity, and these constitute by far the majority of cases. There is no specific medication or treatment for recurrent attacks of pain except rest. The patient usually finds that by resting in bed for one to two days she can greatly diminish the severity of the pain which then spontaneously disappears and never returns.

Follow-up observations on the results of laparotomies performed for psychogenic causes or intermenstrual pain show that the procedure is unsatisfactory and frequently harmful. Some patients may have eight or ten laparotomies and often become addicted to the use of morphine. Others may develop intestinal obstructions which will necessitate one or more operations for correction, and fatalities do occur in these cases.

The true organic lesions causing acute abdominal pain in their order of frequency are: acute appendicitis, intestinal obstruction, whether from neoplasm of the large intestine, intussusception, volvulus or mechanical obstruction of the small gut from bands or adhesions; perforated ulcer of the stomach or duodenum; acute cholecystitis; torsion of ovarian cyst or pedunculated fibroid; torsion of the omentum; and rupture of viscera due to trauma of abdomen.

In these conditions the diagnosis needs no detailed discussion, as the symptoms, physical findings, and laboratory findings are well known to both the internist and the surgeon. Treatment is usually surgical operation either during the acute stage or as an elective procedure. If an operation is to be performed during the acute stage the patient should be well hydrated before laparotomy is done. If the patient has been ill for 48, 72, or 96 hours from peritonitis it may be better to delay the operation for 12 to 24 hours so that a fluid balance can be established; and of course chemotherapy is instituted immediately.

Cases of acute intestinal obstruction should receive special mention in view of the rather general use of the Miller-Abbott tube. I refer to obstructions of the mechanical nature, not obstructions of the adynamic or paralytic type. From my observations at Bellevue Hospital, which has an active ambulance service, tumor of the large intestine and strangulated hernia are the most frequent cause of mechanical intestinal obstruction. The treatment of the latter is obvious and an operation should be performed as soon as hydration permits. Unfortunately patients with tumor of the large intestine causing complete obstruction have been and still are being treated with a Miller-Abbott tube for decompression purposes. This practice should be completely condemned. There is no place for the Miller-Abbott tube in the management of obstruction of the large intestine. Surgical decompression is required in these cases as soon as the general condition of the patient will permit. In the treatment of complete obstruction of the small intestine the Miller-Abbott tube should be condemned. This is also a surgical problem and should be so handled.

The Miller-Abbott tube does have a therapeutic place in cases in which partial obstruction has developed following recent laparotomy. Fresh adhesions may not need a second laparotomy if the intestine can be kept decompressed for several days. The Miller-Abbott tube has a place also in the treatment of adynamic or paralytic ileus.

I should like to mention briefly the significance of abdominal pain due to femoral or inguinal hernia. A small hernia may cause partial or complete obstruction of the small intestine. The hernia may be so small that it is overlooked on physical examination and is not suspected as being the cause of the abdominal pain. A typical patient with such a condition is an emaciated female between the ages of 60 and 80.

Retroperitoneal hemorrhage resulting from trauma may produce severe abdominal pain and clinically an associated paralytic ileus may be present. The retroperitoneal hemorrhage may or may not be associated with rupture of the kidney. In reviewing the traumatic injuries at Bellevue Hospital on two occasions,[4,5] I have been impressed by the number of patients who presented a typical picture of acute "surgical" abdomen although the symptoms resulted from hemorrhage outside the peritoneal cavity associated with reflex ileus. This condition should be suspected if the injury has been over the lumbar region, and there may be evidence of abrasions, ecchymosis, or swelling. Occasionally there may be associated fracture of the transverse process of one of the lumbar vertebrae. The history and physical findings are most important in making a differential diagnosis in this condition. Flat roentgenograms of the abdomen may be misleading as they may indicate fluid levels and cause us to suspect a true organic obstruction, when in reality the cause is a functional disorder of the gastro-intestinal tract and does not necessitate laparotomy.

SUMMARY

Acute abdominal pain can be more accurately interpreted by eliciting a careful history and studying the physical findings than by any other means. The results of laboratory and x-ray studies are frequently misleading and too great reliance should not be placed upon them in evaluating the indications for laparotomy.

The consultant should be given the opportunity to obtain the history directly from the patient. Thus he can better evaluate the symptoms since he is studying an individual and not a case report.

130 East 79th Street.

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The Nervous Woman in Industry

KENNETH D. GARDNER, M.D., *San Francisco*

FOR the purpose of this presentation, a nervous woman is defined as that woman who finds her general well-being impaired because of a state of tension produced by inability to cope satisfactorily with certain conditions or circumstances.

Such a woman is a source of concern to herself since she is unhappy, often frightened of her condition, and, at least in her own mind, frequently ill. She is a source of concern to her employer as her work efficiency is decreased and her absenteeism increased. She is a source of concern to her physician because of the persistency, chronicity, and variety of her complaints.

SOURCE OF MATERIAL

In an attempt to find the underlying causes of nervousness of women in industry, the medical department of a large industrial concern analyzed histories of 25 nervous women over a three-month period. This is not a large series but is assumed representative of the problem, and the data are fortified by years of experience in meeting patients of this type. The medical department referred to is composed of physicians in private practice who spend only part time in industrial practice. As they are not trained in psychiatry or psychology, these observations and conclusions are not those of specialists in these fields.

The business concern here considered does not have hospital or sickness insurance in the usual sense of the term. It does have a sickness disability benefit plan which, after two or more years of employment, provides full or partial pay to employees absent because of sickness. The duration of payments is on a sliding scale and ranges from a few weeks for the two-year employee to a full year for a 25-year employee. In ten of the 25 cases reviewed the employees were declared unable to work by a physician. These women were therefore drawing sickness benefit payments. These ten cases reviewed in a three-month period represented 1,361 days lost from work and $9,580 spent in sickness benefits. The figures are indicative of the loss of time and the cost of disability of this type.

The patients came to the medical department voluntarily, or were referred by a supervisor who noted a health problem, or were interviewed at the request of a company department for determination as to whether or not they were able to return to work.

As the medical department acts only in an advisory capacity, its members were able to observe the methods used by other physicians in management of these nervous patients.

It early became apparent that these women were unable to adapt or adjust themselves to a variety of circumstances, and therefore they will be called "maladjusted." Their complaints were numerous as may be noted in Table 1.

TABLE 1.—*Nature of Complaints Among 25 Nervous Women in Industry*

Complaint	No. of Cases
Nervousness	16
Insomnia	12
Weeping	11
Tachycardia	3
Tremor of Fingers	3
Abdominal Pains	3
Hot Flashes	3
Headaches	3
Dizziness	2
Smothering Sensations	2
Weakness	2
Nauseau	1
Pains in Joints	1
Pains in Neck	1
Pains in Arm	1
Poor Vision	1
Generalized Itching	1
Inability to Decide	1
Hair Falling	1

Nearly every patient presented two if not all three of the main complaints—nervousness, insomnia, and weeping. Once a patient was recognized as probably being in the group of nervous women, an examination was done to determine the presence or absence of organic disease. (Most of them had psychosomatic disease or coincidental organic disease, but only four had active organic disease.) Then an effort was made to discover what were the maladjustment problems. This was in some patients easy, in others most difficult. The best method seemed to be to ask, "Are you happy?" and to watch the reactions. If the answer was negative, the story was easily obtained. Or if affirmative, but associated with hesitancy or vagueness plus moist eyes or actual tears, other key questions such as "Are you happily married?" Do you have any financial worries?" "Are you homesick?" "Do you like your work?" usually elicited the story.

Occasionally a patient will present to the medical department a letter from a doctor to the effect that the patient's work is so nerve-wracking or exhausting that the patient needs a six-month rest. It is true that for physical or temperamental reasons certain types of work may not fit the employee. However, this is usually noted early in employment and a suit-

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able adjustment made. It is rare to find in the case of an employee with relatively long service that the nature of work is at fault. Usually it is found that the employee herself is at fault and has blamed her job unjustly or is hiding another reason for maladjustment. Substantiation for that conclusion is drawn from the fact that in this series there were patients from each of the various kinds of jobs within the company.

As to age of patients, six were in the 15-25 age bracket, four were between 25 and 35, nine between 35 and 45 and six between 45 and 55.

Among the 25 women in this series, those who had been with the firm the shortest time predominated. Eight had been in the company's employ less than five years, four between five and ten years, two between 10 and 15 years, four 15 to 20 years, five 20 to 25 years, and two 25 to 30 years. Eight had severe marital troubles, eight were happily married and nine were single. Most of the women had a high school education or better, seven had had pelvic operations, five had grown up in disturbed home environment.

CASES

In an attempt to condense the various problems of these women and to classify their maladjustments, it was noted that a very important group might be called the "anti-socials." These women were of various ages. They had really never had pleasant relationships with their fellow humans. Some were not able to live harmoniously with their families and had left home as soon as the law permitted. Many had been married and divorced. One had been married and divorced three times. Nearly all lived alone and had few friends, little recreation, and no hobbies. Work was tolerated but many criticisms were directed toward fellow workers and superiors. In brief, these people were unable to get along with anything on two legs. They were all lonely, all overly critical and without realizing it were all thirsty for a companionship that they made no effort to encourage. Seven of the 25 belonged to this group.

Four of the women were classified in the so-called "exhausted state" group. These women for the most part had a heavy burden of outside work, principally housekeeping. The woman in this bracket works eight hours, then goes home to cooking, dishes, and other household chores. On week-ends the husband has a change from the office to, say, a garden; but the wife spends more time in the same old house with more chores. After years of this, she is finally exhausted. Why did she continue working year after year? Usually to gain financially, to own a home, and to enjoy the luxuries an extra pay check represents. Also in this group is the employee who has to care for a sick relative, usually an unmarried daughter caring for a sick or senile mother.

Two of the women in this series were disappointed in love. One young woman experienced smothering sensations dating from the time her boy friend suddenly married a rival. The other, an older woman, could not forget or forgive her husband who had run away with another woman ten years before. Telling of the episode still brought an emotional outburst.

Four were homesick. One of this group found it difficult to adjust to marriage and her first job as well as to leaving home and mother a few thousand miles away. One young woman had left Ireland a few months previously to be in this country with a relative. She disliked the United States, California, San Francisco, the company, and her work. Only the fact that she considered Ireland such a wonderful spot indicated she was not of the "anti-social" group.

Four of the women were not adjusted to their work. It was felt by the examiners, however, that the work was not primarily responsible but that the individual was at fault in not being able to adjust to conditions easily met by others. One woman just starting employment found it difficult to adjust her sleeping and eating habits to evening hours. Another woman feared she might lose her position at a time of great financial strain and as a result had smothering sensations. Another felt she was unable to make decisions. The fourth was upset because in transferring to the West Coast from the East she had given up a supervisory job. "It is much better to give orders than to get them," was her comment.

Four of the women in the series had active organic disease which either played a major role in the maladjustment or confused the picture. One woman who had given two blood transfusions had marked secondary anemia. Rather than weakness and fatigue, the symptoms in her case were insomnia and weeping. In one woman a surgical operation had caused the menopause. Another patient had dysmenorrhea that resisted all treatment and was a source of torment and inconvenience. In another case the presence of a toxic thyroid adenoma hid the real issue. The patient was first seen in 1939 with a clinically toxic thyroid adenoma. It was removed surgically and histologically proved toxic. However, the patient continued to be extremely nervous for several months. It was discovered she was hypothyroid, and there was slow improvement on thyroid medication. Later, however, she became quite agitated, was unable to sleep, and cried easily. In spite of a basal metabolism of −17 per cent and the discontinuance of thyroid medication she continued to be quite nervous. As it was at this time that case histories for this presentation were being obtained, the patient was questioned and it was found that her original trouble started in 1939 at the death of her mother. The patient then had been upset for a prolonged period. Her recent distress was associated with the recognition by her that she had for 13 years been in love with a married man and therefore could not have a home and family which she had dreamed of as a younger girl. At the same time she had been a participant in litigation over an estate. Moreover, she had been living in a five-room house with four adults and had no

privacy or quiet. It was felt by the examiners that the thyroid condition was coincidental and that the basic cause for upset was emotional conflicts.

TREATMENT

In the treatment of these nervous women it must be remembered that the practitioner who has dug out the story of trouble has usually gained the patient's confidence and friendship. Frequent discussions and advice are often necessary. In severe cases or those cases that suggest psychopathic tendencies, psychiatric treatment is of great help.

However, it is not unusual at the mention of a psychiatrist to have the patient reply, "Oh, doctor, I have felt I might be going crazy and now you must think I am, too, because you have asked me to see one of those doctors." Another bar to psychiatric treatment is that many of these women have limited incomes. Part-pay clinics try hard, but our experience has been that they are overcrowded and that personnel changes are so frequent that a patient acquainted with one doctor often has a relapse because she must become acquainted all over again with another. Other persons of great assistance are the company welfare workers, who can cooperate with the doctor in advising and guiding the patient.

Such patients recognize that their work is poorly done, and that is an added cause of anxiety. Few of the patients were benefited by rest alone, but as an escape from work, rest is important. At times a change of environment is most beneficial.

It is quite surprising that there exists such a fear of sedatives in the minds of both patient and physician. Perhaps the lay press has been responsible. We have in fact found the use of small doses of sedatives in the daytime and hypnotics at night to be of great benefit. If the patients can "let down" and can escape the depressing thoughts associated with a wakeful night, a great stride is made toward relief. Risk of addiction or overdosage could be greatly lessened by prescribing small amounts of sedatives at a time, giving definite instructions as to use, and refusing telephoned requests from a pharmacist for permission to refill a prescription.

Excessive use of stimulants is a factor to be considered. In the present series, only two patients used tobacco or coffee to excess. However, one woman not in this series, who had been under treatment for a considerable period because of nervousness, had never been asked and had never volunteered that she smoked up to three packages of cigarets and drank ten to fifteen cups of coffee a day. Excessive use of stimulants is a handicap to the correction of nervousness and should be avoided.

With the exception of the patient with surgically induced menopause, no one in our series found the physiological menopause a primary major upsetting factor although nervous conditions existed coincidentally with the physiological menopause, and in some of the women nervousness was aggravated at the time. Several patients who were given hormone substances, usually by injection, over a period of months or years experienced only moderate decrease in nervousness or no relief at all. The physiological menopause need not cause distressing symptoms. When it does, proper therapy over a reasonable period of time should be effective. If the symptoms are not altered, the case should be re-evaluated, as there are probably other contributing factors.

Attention to general hygiene is an old dictum. It is surprising the number of young women who stay up nights and average only five to six hours of sleep when they should have eight or more. Older women with demanding duties at home may average only a few hours of sleep. Anyone suffering from lack of sleep is potentially a nervous person. To inquire into eating habits may seem foolish, yet one weeping girl (not in this series) had spent so much for clothes that she found it necessary to curtail outlay for food to the point that her daily intake of calories was only 400 to 500. Some of the patients need recreational advice; the need for fun, for companionship poses a serious problem in the lives of many.

PROGNOSIS

In cases in which the nervousness is caused by simple problems and is of recent origin, patients usually can be entirely cured. Optimism is justified if the patient's attendance and attitude record is good and home conditions are favorable. On the other hand, if these are not satisfactory, the outlook is pessimistic. In older people, and particularly in the so-called "anti-social" group, the condition often is irreversible.

CONCLUSIONS

The "nervous woman" in industry usually is maladjusted. Questioning by a physician often will elicit the underlying cause. Sound advice then may restore to fuller usefulness the unhappy person who is a poor worker, a chronic complainer, and a drain on sickness insurance.

2000 Van Ness Avenue.

At the Head of the Table

Wesley Bourne, *Montreal*

Nec solum gens illa sua contenta salute
Excubat hospitibus, contraque nocentia monstra
Psyllus adest populis. LUCAN, IX. 909*

IN the fourth century there lived at Cyrene "a man of many and wandering thoughts" (Mrs. Browning), Synesius by name. Among his writings is a book called *Praise of Baldness*. He reflects that hair is the mark of the beast, that man is in the main bald and that with dogs, the more hair, the less sense. "So the balder a man is, the wiser and the more divine we may take him to be. Hair like the adornment of growing corn withers when the fruit, here the brain, is ripe. Of all shapes the sphere is most perfect—and that is the shape of the bald head," (T. R. Glover's *Life and Letters in the Fourth Century)*. Our head is our most heavenward part. The best of men, priest and philosophers, are all painted as bald. Synesius hoped that the "lovers of hair" (Φιλόκομοι) would be ashamed and adopt the reasonable and honorable practice of shaving, but always pay special honor to those who do not need the barber. This allusion, although rather facetious, is not entirely inapposite to the thought implied by the title of this paper, as it not only draws attention to the relative importance of the human head, but also refers to what goes on within the calvarium of him who officiates at the head of the operating table.

In further simile, witness the influences of the myriad and multiform functionings as they play one upon another, now controlling, now being affected; almost assuring a beauty behind all phenomena; active through them, immanent, beneficent. A good example comes from the recent work of Smith,[8] showing the presence in the cat, dog, and monkey of cortical areas possessing similar cytoarchitectural structure and yielding physiological responses, which presence suggests the existence of a fundamental plan for the cortical control of respiration in the general scheme of cerebral cortical evolution. This observation has been confirmed, indeed, extended by Bailey and Sweet,[1] division of neurology and neurosurgery, University of Chicago Clinics, in their statement that from the orbital surface of the frontal lobe an area in the gyrus orbitalis near the olfactory tract was found to give rise, upon stimulation, to inhibition of respiration, rise of blood pressure and decrease in the tonus of gastric musculature. May these apogean similitudes, in fancy, be given the anesthetist as he uses his senses in endeavor to guide the one who suffers.

We must remember that this quality of keeping watchful guard over the patient has not been acquired exclusively by the anesthetist. He has, in truth, inherited it with gratitude from his predecessors in medicine generally the world about, of whom there are no better examples than the founders of the hospitals, and the medical schools, societies and journals of this your Golden State. Immortal in California medicine[5,6,7] are such names as Father Junipero Serra and Dr. Pedro Prat, pioneers of the eighteenth century; Dr. Richard Den, who answered the layman's question, "What is Mrs. So-and-so's ailment?" with the simple parry, "sickness"; Elias S. Cooper, the founder, in 1858, of the medical department of the University of the Pacific, which in 1908 became the School of Medicine of Stanford University; Hugh H. Toland, founder, in 1864, of the Toland Medical College, which became the Medical School of the University of California; Levi Cooper Lane, who established the library which still bears his name; and Joseph P. Widney, the great educationalist, who incepted, in 1885, the Medical School of the University of Southern California, one of whose deans, Walter J. Barlow, gave the library which bears his name. There are many other exemplars, revered equally by the general practitioner and the specialist.

The epigraph of this essay is taken from Lucanus and would seem not too inappropriately placed as it implies that we belong to a group of individuals who unselfishly keep guard over those who suffer. It draws attention to the exercise of thought and, as well, to the doing of deeds by the anesthetist in the interest of the patient. "At the head of the table" an anesthetist uses his senses momentarily on behalf of the one who is receiving surgical attention. George Malcolm Stratton,[9] professor of psychology in the University of California, from his translation of *Theophrastus on the Senses*, shows that this Greek author pointed out that when the senses are functioning properly, they lead to truth, and that "In the usual course of things perception is 'in accord with nature'; like the knowledge process generally, it is naturally aligned with what is better, working to our advantage, rather than to our confusion and loss." Pascal wrote that "Man is obviously made to think. It is his whole dignity and his whole merit; and his whole duty is to think as he ought."

L'homme est visiblement fait pour penser. C'est toute sa dignité et tout son merite, et tout son devoir est de penser comme il faut.
Les Pensées de BLAISE PASCAL (1623-1662).

Presented before the Second General Meeting of the 77th Annual Session of the California Medical Association, San Francisco, April 11-14, 1948.

Chairman, Department of Anesthesia, McGill University.

*Translation: And that group of persons, not satisfied with safety for themselves, keep guard over sufferers and aid mankind against deadly monsters.

Let us from such *lessons seek and find instruction with an humble mind* (Southey, *His Books)*. Let us envisage a hospital with a department of anesthesia whose personnel is composed of graduates in medicine. Let us visualize these as organized, not only to give service as anesthetists, but also to provide opportunity for the young doctor who desires to learn the subject, so to specialize. There are, already, several such centers of learning and (happily) their numbers are steadily increasing. Of the "voice" of any one of some of these, we may say, in words like those of Sir Arthur Quiller-Couch *(Studies in Literature: The Commerce of Thought, VIII)*, "The fame of it spreads almost as pollen is wafted on the wind: but spreads, and alights, and fertilizes." For a sectional meeting of anesthetists in Kingston, Ontario, I[2] described the three-year diploma course in anesthesia presently functioning in the Department of Anesthesia at McGill University. Let me quote one part of that description:

"In this course the aspirant must have had one year of internship in an approved hospital, preferably in the department of internal medicine. Throughout the three years, the candidate resides in one of six hospitals, moving from one to another every six months. In this rotative manner the individual gains a diversity of experience under the tutelage of many qualified anesthetists. The benefits of this many-sided method of acquiring skill are readily evident, for he who learns from many masters is bound to be more versatile, more Jeffersonian and more percipient than he who ranges under one rubric."

He, who at the head of the table, from an anesthesiological point of view, regulates the state of affairs inobtrusively and in concord with the surgeon, has two main duties to perform: firstly, the conduct of all that has to do with the anesthesia; and secondly, the guidance of those who are in assistance and are there to learn anesthesia. These two offices are fulfilled virtually the one with the other. For example, in a given case, with the pains of taking care to be prepared for eventualities, explanations are given for all that is done. During the operation, the procedure is considered and the occurrences discussed, in soft voice not to distract those at the rest of the table. In the postoperative period, similar vigilant attention is paid to the carrying out of both of these two intensely interesting obligations. Thus may young men learn anesthesia as they help in no small degree. They may say of themselves, with Wordsworth,

> *That we can feed this mind of ours*
> *In a wise passiveness.*
> *Think you, 'mid all this mighty sum*
> *Of things for ever speaking,*
> *That nothing of itself will come,*
> *But we must still be seeking?*
>
> EXPOSTULATION AND REPLY

In the realm of anesthesia, art will little wane, nor will science long lag. Never shall either take to bed, and expire, and be beatified; indeed, never even be

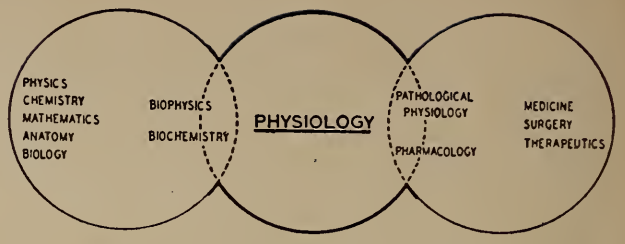


Figure 1

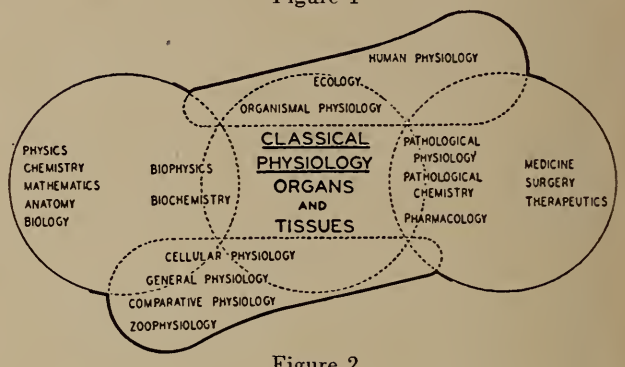


Figure 2

faded, jejune, effete; never, as long as there is confluence of deep thought among young men, in laboratory and in clinic, to face and to solve perplexities; to find and to tap wells more and more abundant, fresh and pure. And, the sources of knowledge are many as they extend to our specialty. One is not long "at the head of the table" before he is convinced of the importance of being familiar with the *classical physiology of organs and tissues* as it still remains squarely in the middle of the picture drawn by Eugene M. Landis,[4] of Harvard University, and reproduced here in Figures 1 and 2 (permission gratefully acknowledged). "This [*classical physiology*] blends in one direction with cellular, general, and comparative physiology, all leaning towards physics, chemistry and biology. At the other end of the scale organismal physiology, ecology and human physiology lean toward pathological physiology and medicine, from which, in fact, many of the truly organismal problems and quantitative studies on man have originated." When we consider that "this multiplicity of subspecialties is a stimulus, an opportunity and a burden, all at the same time," that is, to the physiologist, we should spare no effort in associating ourselves with and learning from him as well as the anatomist, the biochemist, the biophysicist, the pathologist, and the pharmacologist. Also, in practical manner, we should encourage *apt* young physician-anesthetists to become skilled at research and proficient at teaching. Everybody knows that there is at present a direful dearth of anesthetists, and you and I know that many a center is in need of someone capable of guiding a department of anesthesia with regard to the best interest of the patient, the training of personnel and the carrying out of investigation.

And now, speaking of research, we may be assured that there will always be frontiers for inquiry in anesthesia, frontiers wide and deep, to be pierced

following progress in the basic sciences. During the past 15 years especially we have witnessed tremendous advancement in our knowledge of the chemistry and physical chemistry of body processes. We have long known that the remarkable chemical reactions in the cell are brought about by catalysts or enzymes which are capable of accomplishing almost instantaneously feats of synthesis and degradation in an aqueous medium and at 37° C. which in the laboratory cannot be achieved except by prolonged chemical procedures requiring high temperatures and drastic treatment with harsh reagents. It is only recently, however, that the vast accumulation of information concerning these enzyme-catalyzed reactions has been integrated into a coherent science of enzymology. When we consider that each cell contains an array of enzymes which operate side by side and in close coordination, simultaneously building up and breaking down dozens of complex products of metabolism, we can appreciate the delicacy of the equilibrium within the cell and the complex physiological equilibrium between all the cells of the body. Too few of us appreciate how sensitive the cellular enzymes are to disturbances in the composition of the cellular fluid. Very slight changes in the content of water, electrolyte, or metabolites, or the presence of foreign substances may seriously disturb the cellular enzymes. Thus, what we call health is fundamentally a chemical and physiological equilibrium. We all know the severe repercussions of water or salt depletion, malnutrition, hypoxia, renal impairment and so forth, but we seldom think of these diseases in terms of disturbed enzyme function. The action of drugs and the phenomenon of poisoning also are simple manifestations of the interference with normal enzyme activity. When the disturbance becomes severe or prolonged, the damage may be irreparable. The recovery of the patient depends on the restoration of the normal chemical composition of the cell fluids and the recovery of normal enzyme function.*

In the light of these basic considerations, the mechanism of the processes of disease becomes more intelligible. Furthermore, we appreciate how important it is to use drugs with the greatest possible discretion and always to be mindful of the importance of adequate nutrition, of oxygen supply and of the maintenance of salt and water balance.

We learn, too, that the distribution of enzymes in all organisms, be they plant or animal, ameboid or human, is gene-controlled and subject to the laws of heredity. Now and then we meet with an individual who apparently enjoys good health, but who throughout life excretes pentose sugar in the urine, or may excrete phenyl pyruvic acid as a result of some aberration in the metabolism of tyrosine or phenyl alanine. Again, the cells of the black areas of the skin of an animal contain certain enzymes which are capable of producing the black pigment melanin, whereas these enzymes are lacking in the cells of the white areas. Whether certain abnormalities we meet with are caused by the complete lack of one or more enzymes, or a partial lack, or a lack of the enzymes in a specific tissue, remains to be elucidated. Following the same line of observation, we know that individuals by inheritance may possess a predisposition to certain types of failure, or, on the contrary, an exceptional degree of resistance and stability. A knowledge of the individual's family tree is all to the good at any time but is especially important in the field of preventive medicine which is concerned with keeping people well.

The nutritional status of the patient is another consideration that has come to the fore since the days of the late war. Although previously known, it has not been given much attention that the undernourished patient is a relatively poor surgical risk and that the patient in good nutritional condition not only withstands trauma better but makes a smoother and more rapid recovery afterward. It is common knowledge also that the undernourished patient is more liable to liver damage following surgical operation and from drugs. We now realize that in the past we have paid too little attention to the caloric and other nutritional requirements of the patient. We are aware, too, that it is practically impossible to restore the chronically undernourished individual to normal within a short time simply by correcting his nutrition. In future the nutrition of the patient doubtless will be a matter of primary concern.

From the realm of chemistry and pharmacology, the anesthetist can expect an ever increasing number of new agents. While the relationship between chemical structure and biological activity is still obscure, the astounding progress of recent years in the field of synthetic chemistry augurs well for new fundamental advances in our understanding of the action of specific chemical groups or structures on enzyme activity of the cell. Whatever advances may be made in the realm of pharmacology, one should still feel that any biologically active agent ought to be used with discretion. As a general rule the use of any drug should not be expected to correct the basic cause of the disturbance.

Plutarch, the sage of Chaeronea, points out that geographers used to thrust into the extremities of their maps those countries that were unknown to them, remarking at the same time, that all beyond is hills of sand, and haunts of wild beasts, frozen seas, marshes, and mountains that are inaccessible to human courage or industry. This hypothetical method of reasoning may not now be allowed with the dispersing of hyperborean cloud by scientific advances. The anethesiologist will always be interested in the progress of the fundamental sciences, indeed, may often collaborate. Similarly, too, he will keep himself acquainted with all else that goes on in the whole of classical physiology. Has he not turned his attention with enthusiasm to the works of Knisely, Block, Eliot and Warner[3] on *Sludged Blood?* These observers have defined certain prop-

*I am deeply indebted to Orville F. Denstedt, Associate Professor of Biochemistry at McGill University, for guidance in these remarks.

erties of normal blood, of blood flow, and of the vessel walls; have given evidence that these properties are necessary for the functioning of the circulatory system; have described visible responses of the vascular system and/or blood to specific stimuli; have described visible pathological structures and processes; and have set resultant goals for therapeutics. The articles of these investigators are well worth studying inasmuch as they summarize, in part, that their observations, experiments, and deductions supply evidence that the undispersed blood cells provide a common, easily understandable set of factors whereby many diseases can and do damage the bodies of lower animals and of man. They express the hope that as we learn how to keep blood fluid and from becoming agglutinated, or should we say, aggregated, how to keep the vessel walls intact, the red cells from being destroyed, and blood volume adequate; many effects of other pathological mechanisms, in the authors' words, "will stand out clearly, unobscured by the sludge mechanisms. Each will, of course, then receive the undivided attention it merits. The sludges are now ready for study by all the intensive investigative methods our age affords."

The mind of the anesthetist grows accustomed to dwell upon such subjects as I have tried to portray, even, at times, when not at the head of the table. To be sure, I might multiply them and you will agree that they are inextricably intertwined. With training, as time goes on, there comes to the anesthetist, in distinct human manner, the power to see and to know, to feel spontaneously and to think with understanding. He will attain the ἡ ἀθαυμαστία attitude of philosophers, that is, of not wondering at anything; will attain *divine tranquility* which Tennyson defines so well. He might be likened to Louis de Bourbon in the words of Bossuet:

> *Ses partis lui rapportent jusqu'aux moindres choses: on l'éveille à chaque moment; car il tenait encore pour maxime, qu'un habile capitaine peut bien être vaincu, mais qu'il ne lui est pas permis d'être surpris.*
>
> ORAISON FUNEBRE.
> Prononcée dans l'église de Notre Dame de Paris le 10 Mars 1687.

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The Laboratory in the Diagnosis of Communicable Diseases

MALCOLM H. MERRILL, M.D., M.P.H.,* *Berkeley*

MANY of the communicable diseases that formerly constituted a significant proportion of the medical practice of physicians have become all but extinct. Some of these, such as typhoid fever, are so infrequent as to be seen rarely, if at all, in the practice of most physicians. Numerous other communicable diseases occur so infrequently that the specific laboratory procedures available to assist the physician in the diagnosis of these conditions are not generally known. The rarity of these diseases makes their recognition by the physician all the more difficult. Moreover, only recently have specific laboratory procedures been developed to assist the physician in making a definitive diagnosis in a number of communicable diseases, particularly those caused by viral and rickettsial agents.

The cases reported in California during the past five years of certain of the communicable diseases in which specific laboratory procedures are available to assist the physician in diagnosis are given in Table 1. It will be noted that a number of these diseases are reported infrequently. We have no way of knowing how many diagnosed cases are not reported or how many cases occur that are not recognized. In addition, in some instances, such as "Q" fever, the diseases have not been made reportable and our only evidence of frequency of occurrence is acquired by specific epidemiological investigation. Several diseases of frequent occurrence are also listed because they still present practical problems in specific diagnosis in which the laboratory can be of assistance.

TABLE 1.—*Cases of Certain Diseases Reported in California During the Five Year Period 1943-1947.*

Diseases	Cases
Typhoid fever	879
Paratyphoid fever—Total	400
A	35
B	305
C	52*
Type unknown	8
Dysentery, bacillary	1,669
Brucellosis	1,391
Plague	3
Relapsing fever	60
Tularemia	36
Influenza	31,877
Infectious pneumonia	16,208†
Rocky Mountain spotted fever	9
Typhus fever	228
Q fever	178‡
Lymphogranuloma venereum	1,063
Psittacosis	26
Encephalitis:	
Total cases reported	828
Western equine (+ Lab.)	59
St. Louis (+ Lab.)	33
Mump encephalitis (+ Lab.)	9§

*Made reportable July 1, 1946.
†Including atypical and virus pneumonia.
‡Not reportable. Cases found in epidemiological investigations to March 1, 1948.
§Laboratory procedure started July 1, 1946.

The following report deals with the laboratory only as it applies to the identification of the specific infectious agent either by isolation and study of the agent itself, or by the demonstration of the appearance of specific antibodies in the blood serum of the host. The commonly used clinical laboratory procedures, such as blood counts, are not considered in this report.

Several recent outbreaks of some of these communicable diseases have revealed a lack of understanding by the practicing physician of the bacteriological and serological laboratory aids that are available. In several instances there has been an undue delay in the diagnosis of diseases through failure to utilize these available services. Some of the more practical laboratory aids will be itemized herein. This is mostly a review of well-known procedures, but experience in the state laboratory has revealed the need for periodic restatement of the more important procedures. In addition, some of the newer procedures in the viral and rickettsial disease field will also be briefly mentioned, together with an indication as to how these services may be secured.

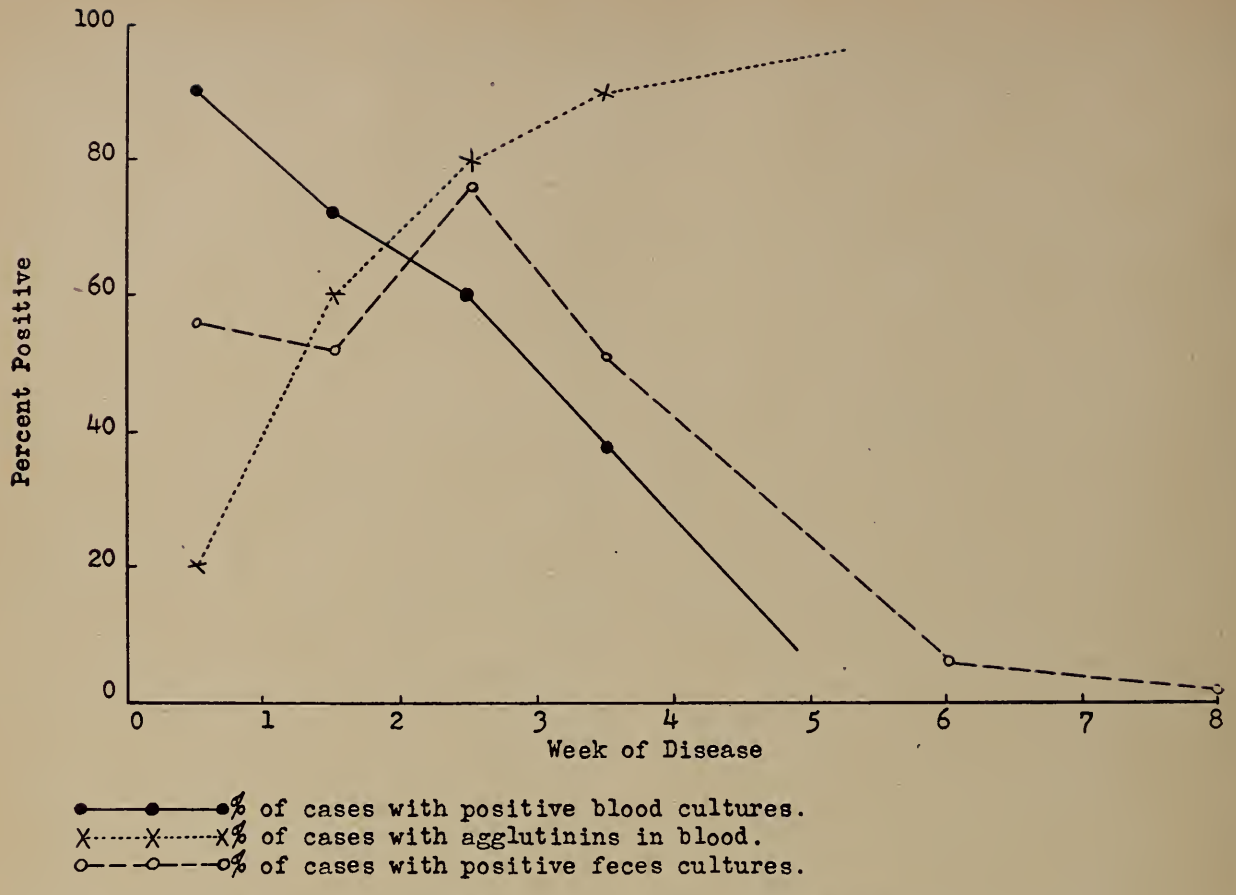
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*Chief, Division of Laboratories, California State Department of Public Health.

TYPHOID AND OTHER ENTERIC FEVERS

Reference to Table 1 will indicate that typhoid fever has become an infrequent disease. During the past five years, only 879 cases have been recorded in California. Physicians may practice for years, or even a lifetime, without encountering a case of typhoid. This results in a low index of suspicion which in turn not infrequently results in a considerable delay in arriving at a diagnosis. In one recent outbreak, involving 21 cases, the onset of the first case was July 3, yet the first case was not diagnosed until July 25, some 22 days later.[2]

In typhoid fever there are three specific laboratory procedures available to physicians. The first is the blood culture, which, as indicated in Chart 1, may be expected to be positive in upwards of 85 per cent of cases during the first week of illness. The second is stool cultures in which the percentage of cases yielding positive cultures progressively increases during the first two weeks of illness. During the first week, however, stool cultures are definitely inferior to blood cultures. The third procedure consists of the demonstration of specific agglutinins in the blood serum of the patient. It will be noted that



Source: Adapted from Topley and Wilson (2d Ed.; 1941), Fig. 259, P 1198.

Chart 1.—Relation of Isolation of Organisms from Blood and Feces and Agglutination Titer in Cases of Typhoid Fever.

agglutinins begin to appear by the end of the first week of illness but that it is the third week before the percentage of cases positive equals the percentage that yield positive blood cultures during the first week of illness. This time-relationship between blood culture, stool culture and serum agglutinin is shown in Chart 1.

Culturing the blood for *E. typhosa* is a simple procedure that can be readily done by any clinical, hospital or public health laboratory. However, many hospital and clinical laboratories lack adequate materials for efficient examination. One of the most frequent errors is the securing of too small a quantity of blood. A good rule is to obtain at least 20 cc. for the culture.

The recovering of the organisms from stool specimens is a more exacting procedure, and not infrequently laboratory personnel not accustomed to the preparation and use of differential culture media used for such isolations will fail to achieve recoveries from positive stool specimens. Local and state public health laboratory services, where workers in general have more experience with this specific procedure, are available to physicians, hospitals and clinical laboratories to assist in such studies.

Agglutinin tests can be done in any well established hospital, clinical or public health laboratory. Satisfactory antigen suspensions for such tests are available through commercial supply houses or from the state laboratory. For epidemiological purposes, the State Department of Public Health requires that cultures of all isolations of *E. typhosa* be forwarded to the state laboratory for phage typing. By this procedure it is possible to separate *E. typhosa* into some eight specific types which appear to be characteristic and constant for any given strain of organism.* This procedure is frequently of much value in determining the source of any given outbreak of typhoid.

All that has been said with reference to laboratory procedures designed to specifically identify typhoid infections applies almost equally well to infections with *S. paratyphosa A* and *B*.

It should also be noted that any one of a large group of organisms of the genus Salmonella may be responsible for acute gastro-intestinal infections in man. These are usually diagnosed as food poisoning by the physician. They are, however, true infections; the symptoms, as far as is known, are due to the infection and not from the ingestion of preformed toxins. Blood cultures are usually negative and specific diagnosis usually rests upon recovery of the specific organisms from stool cultures. In severe infections, there is a rise in the agglutinin

*Recent work by Craigie and Felix has justified the expansion of this scheme to approximately 24 types which according to preliminary work permits a specific typing of 95 per cent of all cultures of *E. typhosa*. Heretofore only 70 per cent could be typed.

titer in the blood stream. However, since the infections are frequently of short duration and transitory, agglutinin determinations are usually of no value in establishing a specific diagnosis. The state laboratory maintains a Salmonella Typing Service for specific identification of any cultures of Salmonella that may be isolated from such cases. From such studies, valuable information is being obtained relative to the occurrence and distribution of the various Salmonella species in California.

BACILLARY DYSENTERY

In California, bacillary dysentery is currently more prevalent than is typhoid fever. There have been 1,669 reported cases in the past five years. This certainly represents the minimum number of cases actually occurring. The true number is undoubtedly far above this minimum. In bacillary dysentery, diagnosis from the laboratory standpoint rests upon the isolation of the specific organisms from rectal swab or fresh stool specimen cultures. Such cultures are almost constantly positive during the acute phases of the disease if correct laboratory procedures are employed. Blood cultures are rarely positive and serum agglutinins appear inconstantly. The many serological cross reactions with other groups of organisms makes the serum agglutinin of little value.

Again the state laboratory has established a typing service which is available for specific identification of species of these organisms. Because of the epidemiological importance of knowing the specific species occurring in the state it is requested that all such cultures be transmitted to the state laboratory.

TULAREMIA

Thirty-six cases of tularemia have been reported in California during the past five years. In this disease, blood cultures early in the course of the disease and demonstration of rise in serum agglutinins after the second week are of value in establishing specific diagnosis. Positive cultures may also be obtained directly from lesions or buboes. These laboratory services are available in all well established clinical, hospital and public health laboratories.

PLAGUE

Plague still occurs in California, although rarely. In recent years only the bubonic form has been encountered, three cases having occurred during the past five years. Direct examination of smears prepared from aspirated material from the buboe with the application of special staining techniques usually demonstrates the typical bipolar staining organisms. Confirmation is secured by culture and animal inoculation. Due to the danger of handling these organisms in the laboratory the regulations of the State Board of Public Health require that the physician or laboratory communicate by telephone or wire immediately with the state laboratory for specific instructions in the handling of material from suspected cases of plague.

BRUCELLOSIS

During the past five years, the number of cases of brucellosis reported has varied from 260 to 320 per year with a total of 1,391 cases. Evidence indicates that this is probably much below the actual occurrence. The laboratory not infrequently provides all too little aid to physicians in the diagnosis of this disease. The only completely definitive laboratory procedure is the isolation of the specific organism from the blood. Of almost equal significance is the demonstration of rise of serum agglutinin titer during the course of the disease, provided there has been neither administration of vaccine nor performance of skin tests. Either of the latter procedures invalidates the results of serum agglutinin tests. In this disease, repeated blood cultures should be made and repeated agglutinin tests performed. The latter are frequently negative during the quiescent stages of the infection only to become positive during acute exacerbations of the disease. Such a rising agglutinin titer provides good evidence of infection, provided, again, there have been no skin tests nor vaccine administration. In this as in other diseases it should be recognized that the presence of serum agglutinins does not necessarily mean current infection. It means either current or past contact with the specific antigen. On the other hand, infection rarely occurs without agglutinins appearing some time at least during the course of the disease.

RELAPSING FEVER

During the past five years, 60 cases of relapsing fever have been reported in California. This is a summer disease contracted for the most part by vacationists in the Sierra Nevada ranges, known cases having been reported from Big Bear Lake in San Bernardino County and from Lake Tahoe south to Sequoia National Park in the central Sierra Range. There is reason to believe that many additional cases occurred which were not diagnosed or not reported. The laboratory methods that establish the diagnosis are the finding of spirochetes of relapsing fever in stained blood smears of the patient or in blood of mice following inoculation with the patient's blood. This service is available in the state laboratory and the larger local public health laboratories and is provided by some of the larger hospital and clinical laboratories.

RICKETTSIAL DISEASES

In California there occur at least three diseases caused by rickettsiae that present diagnostic problems. These are Rocky Mountain spotted fever, which occurs occasionally in the northern Sierra Nevada Mountain range area; endemic typhus, which appears to be limited to the southern California area south of the Tehachapi Mountains; and "Q" fever, which has been identified within the past year and the total distribution of which is unknown. During the past year it has been most prevalent in the Los Angeles area. In all three of these diseases

the definitive diagnosis rests upon either recovery of the rickettsia from the blood taken in the early stages of the disease or a demonstration of rise in complement fixing antibodies as the disease progresses. The latter specific procedure is now largely replacing the long-used, less specific Weil-Felix reaction which rests on a rise in agglutinin titer to certain strains of proteus organisms. Also it should be noted that *Coxiella burneti*, the causative agent of "Q" fever, does not produce agglutinins to "X" strains of proteus. The recovery and identification of the specific rickettsial agent is a time-consuming and costly procedure not without danger of infection to the laboratory worker. However, the complement fixation tests can be readily carried out. Blood should be collected as near the onset of the disease as possible and again a week to ten days later so that the two tests may be run in parallel in the laboratory. A rise in specific antibody is encountered only in the presence of the specific disease. The presence of complement fixing antibodies in a single blood specimen may mean present or previous infection. At present, as far as the author knows, these diagnostic services are available in California only in the state laboratory.

VIRAL DISEASES

There are a number of diseases caused by viruses in which the laboratory can now aid the physician in arriving at a specific diagnosis. Just as in diseases due to bacteria, the laboratory may recover and identify the specific virus or it may demonstrate rise in specific antibodies to the virus in the serum of the patient. The latter, as in rickettsial diseases, is the more simple and practical procedure. The rise in specific antibodies is demonstrated in various ways. One is by the complement fixation test using a specific viral agent as antigen; a second is by the demonstration of virus neutralizing antibodies by observing the effects of properly balanced virus serum mixtures in laboratory animals.

Some indirect procedures have also been developed such as the chicken cell agglutination inhibition reaction in influenza and the occurrence of cold agglutinins in virus pneumonia. Currently such routine diagnostic services in California are offered in the state laboratory. Certain of the tests are also available in a few hospital and clinical laboratories. Such services include tests for influenza, types A and B; virus pneumonia; psittacosis; the various encephalitides due to either Western equine or St. Louis viruses, and encephalitis due to the mumps virus. In addition, complement fixation tests are available for lymphogranuloma venereum and lymphocytic choriomeningitis. In all of these tests the physician should send in both an acute and convalescent blood specimen, the first taken at the earliest possible moment in the course of the infection and the second, ten days to two weeks later.

During the past several years, the State Viral and Rickettsial Disease Laboratory has been studying and developing diagnostic test procedures. As the program during this formative period was largely investigative there were frequently long delays in getting reports back to physicians. Now that a number of the procedures have become routine tests involving complement fixation, results can be reported within a day or two after the second specimen is received. The laboratory diagnostic service available for a number of the viral and rickettsial diseases is therefore now comparable to the agglutination test service available for the diagnosis of typhoid fever. As the various procedures in the viral and rickettsial field are perfected and simplified diagnostic tests are achieved, the services in this field will undoubtedly come to physicians in their own communities through well equipped hospital, clinical and public health laboratories. This will be the case with the more common viral and rickettsial infections; but with rarer infections such as Rocky Mountain spotted fever, psittacosis and the various encephalitides it will probably not be economical for more than one or a limited number of the laboratories in the state to provide such services to the physicians.

SUMMARY AND CONCLUSIONS

It will be seen from the above discussion that the cardinal principles for the clinicians to keep in mind in the diagnosis of communicable or infectious diseases are that an attempt should be made either to recover and identify the specific organism or to provide the laboratory with an acute and convalescent blood specimen so that rise in titer of specific antibodies may be demonstrated. Either of these two fundamental procedures will provide the physician with a definitive diagnosis by the laboratory. As indicated, since a number of these diseases occur so infrequently and the laboratory techniques are new and not readily available, particularly for the viral and rickettsial diseases, the physician must depend for the time being upon the state laboratory for such service. However, as pointed out with the various diseases, in a number of instances services are available through the usual clinical and hospital laboratory channels upon which the physician depends. The logical procedure for the physician to follow is to secure all available services from the laboratory ordinarily serving him, call upon the local public health laboratory for services not provided by his clinical and hospital laboratory, and refer only those specimens to the state laboratory for which no local services are available. At present, the latter are almost entirely limited to viral and rickettsial disease specimens. As this field of laboratory diagnostic tests develops, undoubtedly more and more laboratories will be able to offer diagnostic service in this field.

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The Late Results of Uretero-Intestinal Implantation

Frank Hinman, M.D., *San Francisco*

THERE are three procedures for the permanent diversion of the urine from the bladder—implantation of the ureters to the skin, implantation into the intestinal tract, and nephrostomy. The objections to the first and third are obvious. Very few surgeons now use either when intestinal implantation is feasible. Exstrophy and infiltrating carcinoma of the bladder are the two common abnormalities which require permanent bilateral diversion of the urine. Ureteroenterostomy is now standard treatment for the former and is being used more and more in connection with cystectomy for cancer. There is reason, therefore, to review the late results of uretero-intestinal implantation.

The author's records show that 135 patients, 31 with exstrophy, 84 with vesical carcinoma and 20 with intractable conditions (nine with incurable vesicovaginal fistula, 11 with tuberculous cystitis and with hopelessly contracted bladder) have had ureteroenterostomy. Exstrophy can be successfully repaired after diversion of the urine without aftereffects and therefore gives the best opportunity of knowing the long term survival, the state of health and rehabilitation, after ureteral transplantation in itself.

The late results after transplantation in the other conditions, cancer particularly, are affected by the degree of success in the treatment of the malignant lesion. These facts are of vital importance in the cure of the conditions, of course, but complicate the picture so far as survival from the transplantation itself is concerned. The late results in exstrophy, therefore, give a truer picture of what to expect from the implantation of the ureters into the bowel as a surgical procedure alone. There is, however, this difference: Ureterorectosigmoidostomy usually is done in infancy or early life for exstrophy, but always in late adulthood or even senescence for cancer, and the older patients frequently already have back-pressure changes in the ureters and kidneys which also affect the result. This back-pressure change occurs sometimes in exstrophy when its correction is too long delayed. If there were no recurrence of cancer after transplantation and back-pressure changes were not present in the upper tract before, the late results in the two conditions with normal upper tracts should be about the same except for the difference in expectancy of life. As every child born in this country now has a life-expectancy of over 65 years, operation in infancy permits the observation of a life-span and will tell how long and in what state of health an individual can live after the ureters have been implanted permanently to drain all the urine into such a highly and continuously infected field as the rectosigmoid —requiring adjustment to a state comparable to that which is natural in aves and in some reptilia (ureters opening into the cloaca).

Twenty-five of the 31 patients with exstrophy are living. Four were surgical deaths. Two patients died of acute peritonitis five and eight days after transplantation by the Coffey method before the days of succinylsulfathiazole (1925 and 1930). A modification of the submucous principle,* a principle so well popularized by Coffey in 1912, has been used since 1934 without one instance of peritonitis. This modification consists essentially in anchoring adventitia of the ureter to submucosa of the bowel at the point of its penetration by the ureter. In those patients in whom the wall of either ureter is thin from dilatation, these anchoring sutures cannot be used with safety on account of the risk of puncturing it, with subsequent leakage of urine. The Coffey-Mayo technique has been used as a rule in those instances. With the advent of succinylsulfathiazole, however, the risk of peritonitis is minimal provided whatever method is used is secure against leakage afterwards.

A third patient, four months old, with exstrophy died 2 days after operation and at autopsy, extensive necrosis of the ends of both ureters with leakage was found. The reason for such early operation, namely a relatively sterile bowel, is no longer valid with succinylsulfathiazole and the embryonic condition of the tissues as found in this patient increases the surgical risk. Between one and two years is now thought to be the optimum age for operation. The fourth case, a child of 16 months, died from an anesthetic. With improved methods of preparation and technique (removing the risk of peritonitis), the surgical risk may be estimated conservatively for this group to be well under 5 per cent. The other deaths occurred, respectively, seven years and nine months after operation. The cause of death of the former is unknown. On last examination, five years after operation, he was well, but his mother wrote in answer to a questionnaire after his death: "He had sick spells at intervals when he lost appetite and much weight but had always rallied quickly and built up strength. He was able to attend public school and had just been promoted to the third grade. He was not quite as active as other children, but was well and quite a happy little fellow most of the time." It is probable, therefore, that death followed an attack of recurrent pyelonephritis.

From the Division of Surgery, Subdivision of Urology, University of California Medical School, San Francisco.

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Figure 1.—Photograph of an intravenous urogram taken July 28, 1947. The left ureter was implanted into the rectosigmoid in 1919, the right in 1920 and a plastic repair of the external genitalia was done in 1924. She has been and still is well and active. She married, became pregnant, had an uncomplicated period of gestation and was delivered of a normal child by Cesarean. Urinary control is perfect and nocturia rarely occurs. So far as one can judge clinically, she has never had an attack of pyelonephritis. One could imagine no more perfect result.



Figure 2.—Photograph of an intravenous urogram (a. right; b, left) taken in June, 1946, 14 years after bilateral ureterorectosigmoidostomy at the age of 10 years, showing some hydronephrosis on the right.

The cause of death in the latter case was some form of shock following cystectomy and plastic repair of the external genitalia. The note on her history is as follows: "Patient was returned to the ward in apparent good condition. However, within a very few minutes she became cyanotic, respirations ceased, and she expired. Efforts at resuscitation failed. Permission for autopsy was granted. No cause could be found at autopsy for the child's death. Moderate bilateral hydronephrosis, moderate hydro-ureters. The openings into the bowel were patent, well healed with little inflammatory reaction. There was no gross evidence of pyelonephritis."

Of the 25 patients with exstrophy who are living, 18 have survived more than six years, seven of these more than 10 years and four of these more than 15 years since operation. Of these four, three are in good health 28 years (Figure 1), 18 years, and 15 years (Figure 2) respectively, two with normal-looking ureteropyelograms; the fourth was as well as the others for 20 years and had married but for some unknown reason then began to have attacks of pyelonephritis with pyelographic evidence of urinary back-pressure (the regular follow-up series of intravenous urograms before having been normal). Unilateral nephrectomy and permanent nephrostomy on the other were performed since which the patient has been getting along quite well for the last two years (it is 23 years since the original ureteral transplantation). Another patient surviving 12 years had to have permanent nephrostomy 10 years after operation. and still another 10 years after ureteral transplantation shows well-marked hydronephrosis which may require nephrostomy later. This patient had considerable hydronephrosis when operated on. Some of the remaining 19 patients have occasional attacks of fever, readily controlled by the modern urinary antiseptics, and most of these show varying degrees of ureteropyelectasis, present however in many of them before operation; a majority of the 19 are in good health.

This review of 31 patients with exstrophy of the bladder indicates that a long term survival in good health can be expected after successful ureteral transplantation into the rectosigmoid and the risk of the method therefore does not contraindicate its use in the radical treatment of cancer of the bladder.

Hemagglutination by Viruses—Its Biological Implications

Ernest Jawetz, M.D., Ph.D., *San Francisco*

THE host-parasite relationship in most virus infections is understood poorly because the physical and chemical processes governing the initial virus-host cell interaction have not been accessible to analysis. An understanding of these processes seems of the greatest importance if any advance is to be made in the systematic and not haphazard study of drugs with possible chemotherapeutic action in virus diseases.

The recent literature indicates that progress of great potential significance has been made, permitting a better understanding of the mechanics of some infectious diseases. Research workers investigating the dynamics of hemagglutination by viruses have reported findings which permit a glimpse into the mysteries of virus-host cell relationships. This review presents briefly some of the more important steps in the investigations which led from the discovery of an apparently simple phenomenon, hemagglutination, to the experimental proof that certain chemical substances may interfere with virus multiplication through the blocking of virus enzymes.

The simultaneous discovery by Hirst[14] and McClelland and Hare[21] of the phenomenon of red cell agglutination by influenza viruses was in itself a development of great significance. It provided an exceedingly simple and efficient method of determining the virus content of materials in the test tube, whereas all previous methods were tedious and expensive, using large numbers of experimental animals for virus titrations.

In the hemagglutination test, serial dilutions of virus-containing material are mixed with red blood cells from human, chicken, or guinea pig and the pattern of the settling red cells is observed in 45 to 90 minutes. In the presence of influenza viruses the cells clump in a characteristic fashion. This reaction is specifically neutralized by the serum of immune animals and man. The hemagglutination-inhibition test has formed the basis for the extensive studies on the epidemiology of influenza and the efficacy of vaccines to produce specific antibodies. The methods for this test have been well standardized[23,29] and provide a useful diagnostic tool for the clinical laboratory.

It was believed at first that only viruses of the influenza group possessed this hemagglutinating capacity. Soon it was demonstrated, however,[1,20] that the agents causing two diseases of chickens, Newcastle disease and fowl plague, also agglutinated red cells; and in 1945 mumps virus, grown for the first time conveniently in embryonated hen's eggs,[13] was added to the list.[18]

The mechanism of red cell agglutination appeared similar to that of the clumping of bacteria by specific antisera: The bridges between red cells were virus particles instead of antibody molecules, and the clumps of erythrocytes settling to the bottom of the tube carried with them most of the active virus. A significant difference from ordinary antigen-antibody reactions became evident when it was demonstrated[15] that red cells could be freed from the absorbed virus by incubating them at 37° C., and if resuspended, these same cells could not be agglutinated again by adding fresh virus. The virus eluted at 37° C. from the cells had lost nothing of its infective power or its hemagglutinating ability for other erythrocytes. In fact this virus material could be used over and over again to hemagglutinate and "stabilize" considerable quantities of red cells, suggesting that its activity was that of an enzymatic destruction of the receptor on the cell to which it attached. Subsequently[16] it was shown that similar processes occurred between influenza virus and its receptor cells in ferret lungs. Hirst[16] concluded from this work that the first step in virus-host cell interaction—that is, infection—was an adsorption of the virus to the susceptible cell and subsequent enzymatic destruction of a specific component of the cell surface to which the virus had attached. The nature of this important surface constituent remained unknown for the time being.

Unexpected relationships among hemagglutinating viruses became apparent when Burnet formulated the concept of the "receptor gradient."[21] The observation had been made that red cells treated with one virus and resuspended became inagglutinable by the same virus but retained agglutinability by other agents. This suggested the possibility that each virus might have a more or less specific point of attachment to the cell surface. Once this "receptor" had been destroyed by the action of one virus, only heterologous agents could attach to the cell's remaining receptors. Hemagglutinating viruses could be arranged in a series, indicating their relative affinity for surface receptors: mumps, Newcastle disease, influenza A, influenza B, fowl plague, swine influenza. Red cells resuspended after agglutination by any virus in this "gradient" could still be clumped by any virus following, but had become inagglutinable by viruses preceding it in the series. After agglutination with swine influenza virus, the resuspended cells often clumped spontaneously or when mixed with normal sera. This non-specific red cell agglutination resembled the phenomenon observed by Thomson[27] and Friedenreich[8] in blood specimens

From the Division of Infectious Diseases, National Institute of Health, Bethesda, Maryland, and the Division of Bacteriology, University of California Medical School, San Francisco, 22.

accidentally contaminated with bacteria, especially diphtheroids and vibrios. Substances produced by such bacteria could be adsorbed to, and eluted from, red blood cells, just as with influenza virus, and they similarly changed the character of erythrocytes. Such enzyme-like materials of high potency were obtained from anaerobic bacilli[22] and cholera vibrios,[4] but many other organisms produce red cell agglutination[12] and may form similar products.

The Australian workers[24,3] studied filtrates of cholera vibrio cultures in great detail. It was found that these preparations made erythrocytes inagglutinable by influenza viruses, that they were inactivated by heating, and could be neutralized by specific antisera. They were designated "receptor destroying enzyme"[3] because their enzyme-like action resulted in removal of surface receptors for virus particles and in a change of the surface pattern of red cells: Treated Rh positive cells could be agglutinated by "blocking" as well as by complete antibody, and could be hemolysed by fresh normal guinea pig serum.[24]

In view of the fact that this "receptor destroying enzyme" interfered with the attachment of virus to red cell it was of interest to determine its other effects on virus-host cell relationships. Such studies were performed in animal lung tissue and in the allantoic cavity of chick embryos.[5] It was demonstrated that this enzyme promptly liberated viruses of the influenza group which had been adsorbed to host cells, and that it prevented such adsorption if administered prior to the virus.

Much evidence suggests that this "receptor destroying enzyme" is a mucinase, an enzyme that attacks protein-polysaccharide complexes such as mucin. Several mucins are known to be present on the surface of red cells; and the substance carrying O, A, or B blood group specificity, for example, is a mucin. It was suggested therefore that blood group substances might actually be receptors for virus attachment. Soon it became clear, however,[9,6] that purified O and A group substances did not inhibit hemagglutination and thus apparently did not enter into reaction with the virus. On the other hand several investigators reported a variety of polysaccharides which interfere with hemagglutination or virus multiplication.[11,26]

It appears justified, therefore, to postulate that for the group of influenza-like viruses at least, a polysaccharide, or mucin, on the cell surface may be the point of attachment for the virus. Since adsorption of the virus to the cell surface is probably a prerequisite for cellular infection, the presence of such a polysaccharide may determine whether a cell is potentially susceptible to infection. Support for the hypothesis that polysaccharides are of great significance in virus-cell relationships is provided by the following facts:

1. Hemagglutination by viruses of the mumps-influenza group is inhibited by many more or less complex carbohydrates, from apple pectin to red blood cell extracts.[11,6]

2. The hemagglutination-inhibition effect of various sera[7] is abolished by the "receptor destroying enzyme" and by agents which specifically attack proteins (trypsin, for example) and carbohydrates (potassium periodate). This suggests that the inhibitor in serum may be a polysaccharide-protein complex.[5]

3. Saline extracts of various human and animal tissues inhibit hemagglutination by viruses of the mumps-influenza group.[9] Purified preparations from human red cells and lung tissue which strongly inhibited hemagglutination, proved to be at least 50 per cent polysaccharide by chemical analysis.[6] Filtrates and autolysates of pneumococci (containing much polysaccharide) inhibited red cell agglutination by influenza A virus.[25]

4. Takahashi[26] reported that the multiplication of tobacco mosaic virus could be inhibited by a polysaccharide obtained from yeast.

Most of this evidence is admittedly of an indirect nature, dealing chiefly with the phenomenon of hemagglutination as indicator of the participation of polysaccharides in the early adsorption of virus to tissue cells. Since such chemical compounds are known to occur on cellular surfaces it seems important, however, not to neglect their potential significance.

In studies of bacteriophage-host cell relationships it has been demonstrated clearly with the aid of the electron microscope[19] that adsorption of the virus particle to the surface is the first step in infection of the cell. Such adsorption is chiefly determined by the pattern of surface structures, responsible for the high specificity of these bacterial viruses. That similar specific surface reactions may be important in hemagglutination by viruses is indicated by the following findings: Influenza virus A (PR8 strain) agglutinates red cells of humans and chickens but not of sheep, while mumps virus clumps all three types. Extracts of human cells inhibit all these hemagglutinations, but extracts of sheep cells inhibit only agglutination of sheep cells by mumps virus and not that of human or chicken cells by influenza virus.[6] Thus it appears that the specific inhibiting substance present in the extract (principally of polysaccharide nature) is present on the surface of the cell and may well be responsible for initial virus adsorption.

A similar specific relationship has been demonstrated in a different virus-host system.[28] The susceptibility of animal species to infection with pneumonia virus of mice is proportional to the concentration of a lung tissue component which specifically combines with the virus. Little is known about the chemical nature of this tissue component, but it is interesting to note that multiplication of this virus in susceptible lung is inhibited by several polysaccharides.[17]

The facts presented suggest the possibility that in other animal and human virus infections similar conditions might prevail. It has been proposed[5] that the cellular tropism of viruses may be partly based on the presence of specific chemical sub-

stances on the surface of potentially susceptible cells. The mere presence of this surface structure would, of course, not make the cell susceptible, as evidenced by the presence of specific polysaccharides on red cells which are not invaded by viruses of the influenza group. Viruses possessing enzyme systems specific for such compounds could attach to such cells, whereas cells devoid of these surface structures would be susceptible to virus action.

If it is postulated that a virus has to attach to a specific chemical compound on the cellular surface prior to invasion of the cell, then a corollary postulation might be the possibility of blocking this adsorption by similar chemicals. Materials related to the original enzyme substrate could be administered to the host in order to compete with tissue cells for virus enzymes. Such blockage would offer an excellent method of chemoprophylaxis and chemotherapy of virus infections. Recent reports indicate that this possibility is not altogether idle speculation. Green and Woolley[11] found that several polysaccharides inhibited influenza A virus multiplication in the allantoic fluid of fertile eggs. Horsfall and McCarthy[17] showed that polysaccharide preparations lessened the severity of infection with pneumonia virus of mice and inhibited virus multiplication. Ginsberg, Goebel and Horsfall[10] were able to demonstrate that the multiplication of mumps virus in chick embryos could be inhibited by a polysaccharide from Friedlander's bacillus. Except for the large viruses of the lymphogranuloma-psittacosis group which respond to a number of drugs, this is the first evidence of a useful avenue of approach to the chemotherapy of virus infections. A great volume of work will probably be done in this direction in the immediate future. Even if it should be shown that the effect of polysaccharides is one of competition for virus enzymes not limited to the cellular surface, this would detract little from the value of the stimulation stemming from interest in the mechanism of hemagglutination.

SUMMARY

Some of the more important steps in the investigations on the mechanism of hemagglutination by viruses have been traced. Like pieces of a jig-saw puzzle, apparently unrelated experimental results begin to fit into a pattern which may open the way for better understanding of the dynamics of virus infection of cells and possible approaches to the chemotherapy of virus diseases. The following advances have been most notable:

1. Respiratory viruses of the mumps-influenza group are able to clump red cells by attaching to a specific substance on the cell surface.

2. The point of attachment, or "receptor," is destroyed by enzymatic action of the virus, as well as by enzymes from a number of bacteria and other sources.

3. Enzymes destroying the "receptor" of host cells for this group of viruses, are specific for more or less complex polysaccharides.

4. It is concluded therefore that the virus "receptor" is of polysaccharide nature, on the cell surface. This is supported by the fact that polysaccharides from a variety of sources inhibit adsorption of the viruses to host cells.

5. This primary adsorption is a preliminary step to the infection of the cell. If it can be interfered with, cellular infection can perhaps be prevented.

6. The early interaction of virus and host cell seems to be based on a virus enzyme acting on a specific chemical substrate of the cell. In the group of mumps-influenza viruses this substrate appears to be a polysaccharide.

7. It may be possible to interfere with this enzyme-substrate reaction, thereby preventing early virus action on the cell. This interference may be possible by introducing material similar to the cellular substrate of virus enzymes. Such material, competing for virus enzyme with tissue cells, may provide for effective chemoprophylaxis and chemotherapy.

8. In a few virus infections it has actually been shown that polysaccharides from a variety of sources have definite chemotherapeutic action under experimental conditions.

ADDENDUM

Since this review was submitted for publication much evidence has appeared supporting the affinity of mucoproteins and viruses of the mumps-influenza group. Such mucoproteins were found in egg white and in normal allantoic fluid suggesting a source of error in laboratory tests using hemagglutination techniques. The work on substances blocking the attachment of viruses to host cells has been extended but there has been no further and more definite indication of the chemotherapeutic significance of this mechanism.

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Changes in the Urinary Tract in Pregnancy

Daniel G. Morton, M.D., *San Francisco*

CERTAIN changes occur in the urinary tract in pregnancy which it is important to recognize because they may closely simulate disease. Unless they are clearly recognized for what they are, misinterpretation of their significance may lead to unjustifiably drastic measures and thus much harm to the patient. Beyond the question of proper interpretation, the chief consequence of the changes is an increased tendency to develop urinary tract infection, usually pyeloureteritis.

Autopsy examination and, more recently, pyelographic study have revealed that there is some degree of dilatation of the ureters and kidney pelves in the majority of pregnant women which is most marked between the fourth and eighth months of gestation, but may not disappear completely for four to six weeks postpartum. These changes are more common in the primigravida for reasons that are not entirely clear, but possibly because the tauter anterior abdominal muscles produce a greater pressure of the pregnant uterus against the ureters. The dilatation is usually greater on the right side. The capacity of the kidney pelves may increase from a normal of 5 or 10 cc. to three or four times that amount. In the non-pregnant state such changes would properly be considered pathological. It is this difference which pregnancy is responsible for which is so important to recognize.

A number of structural and functional changes appear to be associated with the ureteral dilatation. Possibly these changes are causative. There is hypertrophy of the muscle cells of the muscular coats, particularly the circular fibers, resulting in considerable thickening of the ureteral walls, most marked in the intraligamentary portions. Since the characteristic dilatation of pregnancy occurs from the pelvic brim upward, and only rarely below this point, and since the dilatation is most pronounced on the right side while the muscle hypertrophy is equally marked on both sides, it does not seem credible that this change can be more than a contributing cause. A functional change of probable prime importance is the loss of tone of the musculature of the ureteral walls. Normally the ureteral walls are constantly engaged in peristaltic activity which is believed to be the mechanism by which urine is moved from the kidney pelvis to the bladder. Traut and McLane have demonstrated that in pregnancy there is a marked diminution in the peristaltic activity, and it is their belief that this is one of the chief factors in the dilatation of the ureters and kidney pelves and backing up of the urine.

The smooth muscle hypertrophy and the atonia of the ureteral walls are most probably responses to the hormonal changes of pregnancy and are similar to the effects which are produced in uterine musculature at this time. It is not strange that similar effects should be produced in these muscular structures, which have such a close embryological relationship. The mullerian duct from which the uterus is derived, and the metanephric duct from which the ureter is descended, first develop in the same mass of mesenchyme on the postero-lateral aspect of the coelomic cavity, and lie almost side by side at that early period in their development when the mesodermal cells become differentiated to become the muscle cells of their muscular coats. The particular hormones which appear to be responsible for these changes are estrin and progesterone, both of which are present in increased amounts during the greater part of pregnancy. Hundley has demonstrated experimentally that estrogens, in addition to their well known property of stimulating hypertrophy of the smooth muscle elements of the mullerian duct system and the closely associated ureters, cause an increase in the peristaltic waves of the ureteral walls. On the other hand progesterone was found to diminish the peristaltic activity of the ureters. These findings fit in with the accepted actions of these hormones upon the uterine musculature and are probably substantially correct.

Mechanical factors probably also play a major role in the production of ureteral dilatation in pregnancy, and indeed they were the first to be incriminated, long before hormones were known to exist. Pressure of the enlarging uterus probably contributes considerably. Dextrorotation of the uterus which is very common may cause some slight angulation of the ureters and thus constitute a factor. In fact dextrorotation plus the difference in the relationship of the ureters to the vessels and the bowel at the brim of the pelvis on the two sides may possibly explain the preponderance of right sided dilatation. Also in favor of pressure of the enlarging uterus being a chief factor in producing dilatation of the upper tract is the absence of such changes in pregnant animals in which the horizontal position of the body removes the possibility of pressure (although the hormonal changes are similar to those found in humans) as well as the absence of dilatation in cases of ectopic pregnancy and hydatid mole in which the characteristic hormonal changes of pregnancy are present without the usual pressure relationships.

The picture which results from these gestational changes is quite distinct—in fact, so distinct as to

From the Division of Obstetrics and Gynecology, University of California Medical School, San Francisco.

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be startling to the uninitiated. In the non-pregnant state dilatation of the degree seen normally in pregnancy would be definitely pathological. It is very important, therefore, for those who have occasion to deal with such cases to recognize the physiological change and to refrain from unduly drastic measures to alter it. I refer particularly to interruption of the pregnancy, the interdiction of future pregnancy, and the like. It must also be realized that some degree of ureteral dilatation during pregnancy may actually be due to a pathological condition. In the presence of repeated urinary infections, permanent damage to the ureteral walls may have occurred; in the form of fibrosis, so that a return to normal cannot take place. It is important, therefore, to repeat visualization of the urinary tract a month or two after the termination of the pregnancy in all cases in which considerable ureteral dilatation has been demonstrated during pregnancy, or in which infection has been repeated or persistent.

Other changes in the urinary tract in pregnancy, such as those which occur in the bladder, have not been discussed because they are of less importance and are not pertinent to the point of this discussion.

SUMMARY

Some degree of hydroureter and hydronephrosis is physiological in pregnancy and requires no action except recognition if infection is not present. Characteristics of the urinary tract changes are reviewed and the importance of recognizing that the changes are not pathologic is emphasized.

General Surgical Complications of Pregnancy

RAY B. MCCARTY, M.D., *Riverside*

GENERAL surgical complications occurring during pregnancy may present formidable problems in diagnosis and treatment. In recent years many former risks to the mother and fetus have been reduced as a result of the accumulated experience in handling these relatively rare cases and by the many advances that have been made in medical science.

In this presentation the more common major, general surgical complications of pregnancy (exclusive of those involving the pelvic organs) will be considered briefly.

ACUTE APPENDICITIS

Acute appendicitis is the commonest abdominal emergency occurring in the pregnant woman. Reports as to incidence vary widely and it is not always clear that only the acute cases are included in the various statistical reports. In five of the reported series studied[2,7,8,22,26] the incidence of acute or subacute appendicitis varied from 17 cases occurring among 16,543 deliveries to 20 cases occurring among 66,431 deliveries. Thus, it is quite obvious that pregnancy does not predispose to acute appendicitis unless there is a history of previous attacks. Most authors agree that recurrent attacks are likely to occur during pregnancy, and in two of the series studied[2,16] the incidence of recurrent attacks was given as 50 per cent and 62 per cent, respectively.

Many authors[2,7,16] report the majority of their cases in the first and second trimester, although in two of the series studied[8,22] the majority of cases occurred in the last trimester. Child and Douglas[7] are of the opinion that actually appendicitis is quite as common in the latter months of pregnancy but that the diagnosis is less frequently made. As they point out, this seems quite logical because the large gravid uterus makes the diagnosis more difficult. Furthermore, the abdominal signs and symptoms that often appear late in pregnancy are difficult to evaluate. Although many attacks of acute appendicitis subside spontaneously and may not have been recognized, it is significant that most series show that the majority of cases of ruptured appendix with attendant serious complications occur in the third trimester.

A ruptured appendix is much more serious in the pregnant woman due to altered anatomical relationships and physiological changes. The omentum and loops of intestine which usually assist in the process of localization are crowded out of the way by the growing uterus, the appendix and cecum may be displaced upward after the third month so that pelvic localization is less likely in the ruptured appendix, and the uterus tends to prevent localization due to its changes in position. These factors, together with physiological increased vascularity and lymphatic dilatation, greatly favor a generalized peritonitis with absorption of septic material, abortion or premature labor and possible death to the prospective mother.

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Success in the treatment of acute appendicitis depends on early diagnosis and prompt removal before rupture of the appendix. The earliest symptom is pain, at first epigastric and later shifting to the right lower quadrant, but this pattern may vary as in the non-pregnant patient. Nausea and vomiting may or may not occur. A slight to moderate fever may be present.

Localized tenderness over the region of the appendix, the most consistent sign of appendicitis, must never be regarded lightly. Involuntary muscle spasm may or may not be present. In evaluating the abdominal tenderness it is well to remember that, in some cases at least, the appendix is displaced upward. Baer[2] and his associates, in a roentgenological study of 70 pregnant women with normal appendices, found that in 88 per cent the appendix was located above the iliac crest after the seventh month. Twyman, Mussey and Stalker,[28] however, in reporting on 75 cases of appendicitis during pregnancy state that at operation, "marked displacement of the appendix was not evident in most cases." It must be remembered that pregnancy is accompanied by a physiological leukocytosis and that a normal white count may be as high as 12,000 to 15,000. An increase in the polymorphonuclear cells, however, is significant. A very helpful diagnostic point is the history of previous attacks and, since this is a particularly significant point in pregnancy, the patient should be carefully questioned in this regard.

A larger percentage of erroneous diagnoses of acute appendicitis in the pregnant woman is to be expected because of the gravid uterus and the multitude of abdominal signs that occur, particularly late in pregnancy. However, because of the seriousness of a ruptured appendix in the pregnant woman, the surgeon must always be on the alert and never procrastinate where he cannot reasonably rule out the condition after a careful differential consideration. Occasionally a normal appendix will be removed or another pathological condition found if this policy of earlier and more frequent operation is carried out, but, as demonstrated by Child and Douglas[7] in their series, "mothers do not die nor are babies lost as a result of an uncomplicated celiotomy."

Careful management of anesthesia is required in the surgical treatment of any complication of pregnancy, and of especial importance is the administration of an adequate amount of oxygen at all times whether the anesthesia is spinal or general.

If one is reasonably sure of the diagnosis of acute appendicitis, a McBurney incision placed over the point of maximum tenderness seems wise even in those cases in which the patient is near or at term. By using this incision one is less likely to disturb the uterus and intestines and the danger of postoperative intra-abdominal and wound complications is less. With the aid of the sulfonamides and penicillin, intra-abdominal drainage is not resorted to as frequently as in the past, but is indicated in the rare case of an old abscess with a thickened necrotic wall, or in a case of general peritonitis where the appendix is not readily located and therefore not removed. Soft drains should be used and they must be placed so as not to come in contact with the uterus or be disturbed by the changes in the position of the uterus.

It is generally agreed that in cases of acute appendicitis the obstetrical factor is to be entirely disregarded except, as Cosgrove[8] has said, the "recognition of the very rare possibility of concurrent serious factors of obstetric dystocia. When this occurs, recourse may be necessary to delivery by the abdominal route. But such interference should be reserved until after the onset of spontaneous labor, and an extraperitoneal approach selected."

Postoperative care differs very little from that given non-pregnant patients, except that sedation and progesterone are used to forestall abortion or premature labor, and enemas and cathartics are avoided for at least four or five days after operation.

GALLBLADDER DISEASE

Since cholelithiasis occurs at least three times more frequently in the female than in the male and 80 to 90 per cent of cases occur in women who have been pregnant at least once, pregnancy has been considered a major factor in the development of this condition.

Biliary stasis and increased blood and biliary cholesterol would appear to set the stage for the development of cholelithiasis in women who have been pregnant. By cholecystographic studies, Gerdes and Boyden[11] have clearly shown that in the second and third trimesters of pregnancy the emptying of the gallbladder is retarded. They attribute this to a "hypertonic condition of the sphincter choledochus, i.e., to a physiological dyskinesia reflecting the changed hormonal content of the organism in pregnancy."

Potter,[24] by direct examination of the gallbladder in a large number of patients delivered by cesarean section at term, found that 75 per cent of normal gallbladders were distended. An analysis of the contents of 58 of these distended gallbladders, withdrawn by means of a sterile needle and syringe at the time of operation, revealed a high cholesterol level and a relatively low bile salt concentration, which is similar to the chemical findings in a damaged gallbladder. As noted, these findings were all in connection with supposedly normal gallbladders and it would appear from these changes and the stasis that there may be damage to the gallbladder wall with alteration of the concentrating power of the mucosa and eventual precipitation of cholesterol. It is worthy of note that Potter[24] rarely found bacterial invasion of the gallbladder bile at term.

Medical management of cholecystic disease can usually be carried out successfully during the course of pregnancy. However, if the patient is subject to repeated attacks of severe gallstone colic, surgical operation is indicated in a quiescent interval if possible. The danger of empyema with possible result-

ant perforation must always be considered and operation done immediately if this condition is suspected.

In the uncomplicated case of cholecystic disease without peritonitis the risk of operation is no greater in the pregnant woman than in the non-pregnant, and cholecystectomy is generally the procedure of choice. However, cholecystostomy is indicated if the patient presents an added risk because of peritonitis or systemic disease, or if there are unusual technical difficulties in removal of the gallbladder. In upper abdominal operations the risk of abortion or premature labor is very small unless peritonitis has developed.

INTESTINAL OBSTRUCTION

Intestinal obstruction occurring during pregnancy is an infrequent but always serious complication. It is most often due to adhesions from a previous operation or adhesions resulting from a previous intra-abdominal inflammatory process. The changing size of the uterus naturally changes the normal relationships of the abdominal viscera, so that adhesions that previously were of no significance may cause kinking and obstruction. Statistics show that the obstruction may occur at any time but is most frequent from the fourth to sixth month of gestation, late in pregnancy and at the time of labor, or in the early days of puerperium.

Some of the less frequent causes of intestinal obstruction in the pregnant woman may be:

1. Congenital adhesions or, very rarely, a congenital defect in the mesentery or broad ligament.

2. Volvulus, which usually occurs in the presence of an abnormally long mesentery and/or improper rotation of the intestines. In 79 cases that have appeared in the medical literature, as reported by Kohn and his co-workers[14] in 1944, the obstructions were localized as follows: "small intestine, 19 cases; large intestine, other than sigmoid, 19 cases; sigmoid, 41 cases."

3. Carcinoma of the large intestine: In 1947 Swartley and his co-workers[27] reported a total of 71 such cases in the literature, including one of their own.

4. Intussusception: In 1937 Chaffin and co-workers[5] collected reports of 19 cases from the literature and added one case of their own in which obstruction was caused by adenoma of the jejunum. In only one other case among the 19 is tumor within the bowel noted, but, as the authors state, "probably such neoplasms were overlooked in some of the cases with undetermined etiology." Enteric ulceration from tuberculosis was a prominent cause.

5. Hernia: This is much less common as a cause of intestinal obstruction than one would suppose. The enlarging uterus pushes the intestines away from the inguinal and femoral canals and most of the reported cases have been due to umbilical and incisional hernias.

6. "Pregnancy ileus": This is merely an intestinal occlusion caused by the growing uterus pressing the sigmoid colon against the brim of the pelvis. The existence of obstruction of this type is probably questioned by many obstetricians and surgeons but it appears to have been firmly established as a rare clinical entity. Ludwig (1913)[15] collected reports of ten cases, Mikulicz-Radecki (1926)[19] collected ten cases, and Eliason and Erb (1937)[10] collected 25 cases from the literature during the period from 1925 to 1935 and added three of their own. Practically all pregnant women are constipated and, as has been pointed out, if there were an added disturbance of the vegetative nervous system "pregnancy ileus" might occur in the later months of pregnancy.

The diagnosis of intestinal obstruction in the pregnant woman is most difficult because many of the cardinal symptoms of obstruction may be seen in normal pregnancy. If the condition is suspected, every facility possible must be used to reach an early decision if one is to avoid the danger of peritonitis with its attendant high maternal and fetal mortality rate. An evaluation of the past history regarding previous operations or previous abdominal or pelvic complaints is important along with a careful appraisal of the present history, physical findings and laboratory studies. An x-ray film of the abdomen to determine the gas pattern is always indicated, although the evidence may not be conclusive. If no gas is found in the small bowel and the symptoms suggest obstruction in the large bowel, sigmoidoscopic examination and/or a barium enema is indicated, depending on the suspected site of obstruction. If the barium enema meets obstruction in the pelvis a tumor is the most likely cause, although the rare possibility of "pregnancy ileus" as a cause of the obstruction arises and, as a diagnostic measure, an enema given in the knee-chest posture is indicated. In two of the three cases of "pregnancy ileus" reported by Eliason and Erb[10] the obstruction was relieved in this manner.

Generally speaking, spinal anesthesia is the best in connection with operations to relieve bowel obstruction as better relaxation is obtained, and thus there is less trauma involved in handling the bowel. In the presence of bowel obstruction one of the greatest anesthetic hazards is the danger of aspiration of regurgitated material. McCuskey[17] states that this can be minimized by using spinal anesthesia preceded by light medication so that the patient is able to cough and keep the trachea clear; or, if a general anesthetic is given, an endotracheal catheter may be used with a balloon attached to completely seal off the trachea.

The surgical results vary directly with the promptness of operation. Simple freeing of adhesions requires little manipulation so there is small danger of peritonitis in the early case and the pregnancy is endangered very little. However, when operation has been delayed, permitting vascular changes that make resection necessary, the dangers mount rapidly. In Eliason's and Erb's[10] collected series of 66 cases of intestinal obstruction covering the period

1925-1935 the maternal mortality rate was 21 per cent and the fetal death rate 50 per cent.

In a consideration of carcinoma of the large intestine Swartley and his co-workers[27] expressed the opinion that there is not enough evidence to support the idea that pregnancy affects an extragenital malignancy to the extent that termination of the pregnancy is indicated. It is quite generally agreed that in early pregnancy the management of the carcinoma should be the same as in the non-pregnant patient. As to carcinoma in the later months of pregnancy, Bonner and his co-workers[3] and Swartley[27] recommend exploratory laparotomy to determine operability. If the carcinoma proves inoperable and there is no obstruction to the birth canal, colostomy is done to permit normal delivery. If operation is feasible and manipulation of the female organs is necessary, cesarean section, hysterectomy, and resection of the lesion are carried out in one or two stages. This eliminates the possibility of miscarriage with the increased risk of peritonitis. When the lesion is outside the pelvis and manipulation of the female organs is not necessary, an exteriorization procedure or an end-to-end anastomosis may be carried out, permitting normal delivery. These radical procedures are carried out, of course, only in cases in which it may be assumed that the obstruction is only partial. Before operation the bowel must have been decompressed by the use of enemas, and there must have been adequate preoperative preparation with sulfasuxidine or sulfathaladine. If the obstruction is complete, as occurs in a very small percentage of large bowel malignancies, colostomy is the only safe procedure and it is to be carried out as a preliminary or final procedure. As in other surgical emergencies of pregnancy, progesterone and sedations are indicated postoperatively.

HYPERTHYROIDISM

A physiological enlargement of the thyroid gland occurs in many pregnant women, as the state of pregnancy demands an increased secretion from this gland. Various observers are essentially in agreement that the basal metabolic rate remains normal during the early months of pregnancy and then, gradually rising in the last three or four months, reaches 20 to 25 per cent above normal at term. This increased rate indicates the response of the thyroid gland to the increasing mass of active protoplasmic or fetal tissue and, to a lesser extent, to an increase in the maternal structures incident to pregnancy.

Although it is not uncommon for pregnant patients to present evidence of nervous instability, careful evaluation of the subjective and objective findings usually will not substantiate a diagnosis of hyperthyroidism which is a relatively infrequent complication of pregnancy. Various statistical reports as to incidence of this disease during pregnancy show a variation from .07 per cent to 3.7 per cent, and in general it is more frequently seen where goiter is endemic.

Of the two distinct diseases of the thyroid gland associated with hyperthyroidism, exophthalmic goiter is found more frequently as a complication of pregnancy than adenomatous goiter with hyperthyroidism.

The normal course of exophthalmic goiter is subject to exacerbations and remissions. Frequently it can be managed through pregnancy with the judicious use of compound solution of iodine (Lugol's solution), sedation and rest. An index which can usually be followed cautiously is that if a mild case of exophthalmic goiter responds with a remission after two weeks of treatment, the patient can usually be carried through the pregnancy in a conservative manner. If the response is not practically or entirely complete, subtotal thyroidectomy is usually indicated except in selected cases in the last trimester of pregnancy.

Adenomatous goiter with hyperthyroidism usually has the tendency to become progressively worse and does not often show a good response to iodine. As is emphasized by Mussey[20] and others, it is usually advisable for the patient to have the adenoma removed. As Mussey[21] states: "Even in the last six weeks of pregnancy, in the presence of a metabolic rate of more than 50 per cent [above normal] which has been maintained for a considerable period, in the presence of myocardial insufficiency or of dyspnea caused by pressure of the adenoma on the trachea, removal of the adenomas prior to delivery of the baby usually is the safest procedure." Also in a case of multiple large adenomas without hyperthyroidism where substernal pressure on the trachea is present it may be advisable for the patient to have the adenomas removed.

Each case must be individualized and, as McLaughlin and McGoogan[18] state, "there can be little doubt that the pregnant woman with hyperthyroidism can successfully withstand a thyroidectomy, but the question remains the necessity and advisability of the procedure in all cases." In the rare instance in which there has not been an adequate response to compound solution of iodine and in which surgical operation is considered too hazardous, x-ray therapy may be tried.

Therapeutic abortion is practically never indicated for hyperthyroidism, as is emphasized by Mussey,[20] Portis and Roth,[23] Baumgartner[4] and many others. In mild cases abortion needs no consideration. In severe cases the possibility of a thyroid crisis arises; abortion does not cure the hyperthyroidism.

The use of Thiouracil and kindred drugs in hyperthyroidism has been modified considerably since their introduction due to some of the severe toxic reactions that have resulted. In the pregnant woman transfer occurs across the placental barrier and hyperplasia of the fetal thyroid has been demonstrated. Also the drug appears in the mother's milk. As Curtis and Swenson[9] state, "Carefully controlled studies on the experimental animal and in man are not yet available to judge the effects of such long continued therapy accurately on either the mother

or the fetus. Widespread use of the drug during the period of gestation should be avoided until further studies are available unless the emergency is dire."

CARCINOMA OF THE BREAST

The development of carcinoma of the breast during pregnancy is fortunately an infrequent occurrence. If it does occur a fulminating growth is likely, as the breast is being prepared for lactation by an increased hormonal stimulation which results in an increased blood supply and a large increase in the glandular and ductular elements. Harrington,[13] in a study of 92 cases in which the tumor was present in the course of pregnancy or lactation, found that in 81.5 per cent the tumors were of either grade III or IV malignancy and that in 84.8 per cent of the cases there was axillary involvement at operation. In this series the five-year survival rate for patients with axillary involvement was 5.7 per cent. However, in those few cases in which there was no axillary involvement the five-year survival rate was 61.5 per cent, which indicates that the condition is not hopeless if recognition is early. Thus, from these grim figures, it is obvious that the obstetrician must be on the alert and make frequent routine examinations of the breast during pregnancy.

If any suspicious discrete mass is found in the breast, removal of the mass and microscopic examination are obligatory; and if it is found to be malignant, radical mastectomy is indicated. Also, because of the usual high degree of malignancy in these cases, x-ray therapy seems indicated regardless of whether the axillary glands are involved or not. Some observers consider all cases which occur during pregnancy or lactation to be inoperable due to the high degree of malignancy.[12]

The question of whether the pregnancy should be ignored in the presence of carcinoma of the breast is important. If the pregnancy is not interrupted most patients will go to term and deliver a normal child even after submitting to a radical mastectomy and x-ray therapy. In the past most obstetricians and surgeons have individualized their treatment of cases but generally have been of the opinion that the pregnancy should be ignored in the presence of carcinoma of the breast. It would appear from Smith's[25] statistical study of a small group of pregnant women with carcinoma of the breast that the prognosis is better if the pregnancy is not interrupted. Recently, however, Chase[6] has advocated interruption of the pregnancy followed by testosterone, radical mastectomy and x-ray therapy. Testosterone has demonstrated its palliative value in many cases of bony metastasis from carcinoma of the breast but only occasionally has a favorable palliative response been noted in the case of a primary tumor or metastases from it to soft tissue. As Adair[1] has pointed out, the field of androgen therapy in carcinoma of the breast is new and a great deal more clinical research must be carried out before a final evaluation of it is made.

3616 Main Street.

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Chemotherapy for Renal Infections

Donald A. Charnock, M.D., *Los Angeles*

Chemotherapy for renal infection has advanced tremendously during the past decade. This has stimulated the growth of a voluminous literature. Out of this plethora of data there is emerging some definitive information which will aid in the treatment of pyelonephritis. If we speak in the main of the better established clinical aspects of renal infection, we do so with full knowledge of the many gaps in our understanding of the basic principles underlying the mode of onset, the pathways of entry and the actions of the bacteria which cause pyelonephritis. Moreover, our understanding of the mechanism of chemotherapy is still fragmentary.

The use of the newer chemotherapeutic agents has greatly increased the effectiveness of treatment but it has not simplified the process. Proper use of these drugs requires intelligent knowledge of various factors which, even today, are too often neglected.

The choice of chemotherapeutic agents in the treatment of renal infections is determined by the type of bacteria found in the urine. While the kidney may be the victim of practically any of the pathogenic organisms, five main groups will encompass the bulk of urinary infections. These, in order of their prevalence are: (1) The E. Coli group, (2) the staphylococcus, (3) the streptococcus, (4) the proteus and (5) the tubercle bacillus. Mixed infections frequently occur. Moreover, cases of typical pyelonephritis have been described in which no causative organism may be demonstrated.[8]

The first principle in obtaining an accurate understanding of the bacteriology of infected urine is proper collection of the specimen. Neglect of this is one of the most common causes of error. The specimen must be fresh and collected in clean containers. In the female patient, a specimen taken by catheter is essential. In the male patient, a carefully collected second glass specimen is usually sufficient. For a complete study, urine catheterized from both kidneys is necessary.

The initial step in the study of the urine is the examination of the fresh urinary sediment; this is followed by staining. The simple stains will give much information. The Gram stain affords more differentiation. Where tubercle bacilli are suspected, special staining must be carried out. Cultures should be used for confirmation of the microscopic findings and for separation of the bacterial sub-groups. Treatment may be initiated on the basis of the microscopic information. Only in special instances should therapy be held up for the more elaborate cultural differentiations. Criteria of cure, of course, are negative cultures.[14]

Brief mention must be made of the determination of the reaction (pH) of the urine. While there is little of diagnostic value in this test, it is of essential importance in intelligent chemotherapy.

Accurate knowledge of pathological processes coexisting within the urinary tract is paramount.[13] Good renal function with absence of foreign bodies and ulcerative lesions, together with free flow of urine, is essential to successful therapy. Simple tests may be used to determine these factors. Renal function may be accurately determined either by blood nitrogen levels or by the excretion dye tests. Simple and rapid estimations of function may be obtained by specific gravity observations. Foreign bodies may usually be picked up by roentgenographic flat films. As a rule, destructive lesions and evidence of obstruction may be determined by excretory urograms. For exact reviews, where definitive pyelographic outlines and collection of urine for bacteriologic and differential functional studies are required, the retrograde cystoscopic examination is necessary. As a rule, the more persistent the infection, the greater must be the effort in evaluating coexisting disease.

EFFECTIVE CHEMOTHERAPEUTIC DRUGS

The present effective chemotherapeutic drugs are mandelic acid, the sulfonamides, penicillin and streptomycin. Each has its role in modern therapy. Their efficacy is in direct relation to the concentration of the drug in the urine and in the tissues. This, in turn, depends upon the dosage, the renal function and the renal volume.[13]

Mandelic acid is effective against the E. Coli, streptococcus fecalis and occasionally against staphylococcus albus. In order to be effective, the urinary concentration must be 0.5 per cent or greater and the urinary pH must be 5.5 or less. It may be given in liquid or tablet form. It is usual to include ammonium chloride as an adjunct. The fluid intake should be limited to 1,200-1,500 cc. daily, and alkaline foods, especially fruit juices, should be omitted. Mandelic acid is contra-indicated in acute pyelonephritis, in cases of decreased renal function and in the presence of high fever. It is not well tolerated in older patients.[9]

The sulfonamide family was the first of the magic bullets. In urinary infections the sulfonamides are effective against all the commonly occurring Gram negative bacilli, the staphylococcus and occasionally, the streptococcus fecalis. Sulfathiazole and sulfadiazine are more useful than the earlier forms.

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The toxic manifestations due to the sulfonamides are well known. They are less frequent with the newer forms. Crystalluria is increased with sulfathiazole and sulfadiazine. Most alarming are the renal complications which result from the poor solubility of these drugs and their acetyl derivatives. This may result in anuria. Two types have been noted, the mechanical anuria in which occlusion of the renal collecting system may result from precipitation of crystals or concretions, and the chemical anuria which is due to acute toxic and degenerative lesions of the renal tubules.[1]

In the treatment of urinary infections the dosage of the sulfonamides may be kept below the critical level at which most of alarming complications occur. Doses of 2 gm. daily for the first two days, then 1 gm. daily for 14 days will usually result in sterilization of the urine in cases where the bacteria are susceptible and there are no complicating uropathies. The question of adjuvant alkali therapy is still under investigation. The majority of studies indicate that alkaline urine increases the solubility of the drug, thus reducing the incidence of renal complications.[5,11,17] At present, it is our practice to give sodium bicarbonate in equivalent amounts with each dose of sulfonamide. In cases of renal or cardiac insufficiency the use of alkali therapy may present a difficult therapeutic problem. Here one must weigh the possibility of edema from the sodium ion against the consequence of renal damage.[1]

Fluid intake with the sulfonamides should range from 1,500 to 2,000 cc. daily. The urinary output must be measured and the drug stopped if the level falls below a litre daily. While crystalluria does not necessitate withdrawal of the drug, it calls for increased vigilance with respect to the possibility of renal damage. The combination of two or more sulfonamides has made it possible to give relatively large total doses of the drug with little tendency to crystal formation.[21]

Relapse following sulfonamide therapy has been noted. It is not so frequent as found with either penicillin or streptomycin. It has been our experience that sensitization to the drug is not so marked as with the newer antibiotics. As a rule the organisms respond equally well to further sulfonamide therapy.

Penicillin is largely eliminated by the kidneys.[2] The amount depends upon the dosage, the method of administration and the renal function. This takes place apparently by filtration through the glomeruli and excretion by the tubules.[20] The excreted penicillin possesses antibacterial properties.[22] This gives a high level of the drug in the urinary channels. It is certain that the blood supply to the tubules contains a higher level of penicillin than is found in the peripheral circulation. This high level within the renal circulation and the urinary channels results in the effectiveness of penicillin in urinary infections.

The mechanism of action of penicillin has not been proven. Studies indicate that it is the result of an interference with a metabolic function concerned in the early stages of bacterial multiplication.

From a clinical standpoint, penicillin has become the most effective agent against the staphylococcus and the streptococcus. Most strains of these two groups are either highly or moderately susceptible. The bacillary group and the streptococcus fecalis show little or no susceptibility. This has been shown to be due to the production by these organisms of a substance capable of inactivating and inhibiting penicillin. Because of the enzymatic nature of this agent, it is called penicillinase. The E. Coli group are particularly capable of producing penicillinase. It is due to this activity that oral and rectal administration of penicillin is of reduced therapeutic value.[20]

Various routes of administration have been studied. At present the usual practice is to use intermittent intramuscular injections. With aqueous solutions, absorption is fairly rapid and there is still an effective concentration in the blood at the end of three to four hours.[27] Our present practice is to administer 25,000 to 50,000 units at intervals of three hours around the clock. Evidence indicates that a four hourly interval will give comparable clinical results. Where the ambulatory patient is being treated, penicillin may be administered in the wax and oil vehicles.[27] The average dose is 300,000 units in 24 hours. Recently, the combination of penicillin with procaine in an oil base has proven very effective.[12]

ORAL ADMINISTRATION OF PENICILLIN

Oral administration of penicillin has been widely used. Effective serum levels may be secured and maintained. The penicillin is absorbed from the stomach and duodenum. It is best given on an empty stomach and the dosage must be several times larger than with the intramuscular route. The present cost of the oral form is still high. This will undoubtedly be reduced in time. Dosage of 100,000 units every two to three hours is advocated.

In urinary infections we feel that medication should be continued for five to seven days. If sterilization of the urine has not been accomplished in this time, it must be assumed that the bacterial strain is not susceptible or that urinary stasis or reduced renal function has prevented the drug from acting upon the organisms. We recognize the value of susceptibility tests upon the bacteria, and where this is practical it should be done. The use of penicillin is not incompatible with the sulfonamides. The combination of the two drugs will prove very helpful in combating mixed infections. There have been some reports indicating a synergistic action between the two drugs.[30]

The toxicity of penicillin is remarkably low. High dosage has resulted in some urticarial and skin reactions. This is most likely to occur with the administration in the oils and beeswax preparations and is probably a reaction to the vehicle rather than to the penicillin.

The use of various preparations to increase the blood levels of penicillin depends upon blocking tubular excretion. While this may be valuable in other systemic diseases, it seems unnecessary in renal infection where excretion through the tubules is beneficial.

Relapse following penicillin is more common than with the sulfonamides. Resistance of the organism can occur. It is not so pronounced as with streptomycin.

Streptomycin was first described in 1944.[28] It was found to be most effective against the Gram-negative bacilli.[26]

Streptomycin is measured in terms of weight of the pure substance.[19] Following parenteral injection, streptomycin is readily absorbed and reaches the urine within one to three hours. Between 60 and 80 per cent is eliminated by the kidneys.[3,4] The rate of renal excretion is slower than for penicillin, probably because streptomycin is eliminated by glomerular filtration alone and does not seem to be excreted by the tubules.[6,25] Levels of the drug in the urine are much higher than those found in the blood. It is interesting that streptomycin in concentrations higher than 200 micrograms per cc. reduces Benedict's solution. This may be used as a rough index of urinary concentration.

In view of the wide variation in susceptibility of organisms and their various strains to streptomycin, it is advisable to determine the sensitivity of the infecting strain as a guide to treatment.

In renal infections, streptomycin is best administered by intermittent intramuscular injections. The dosage depends upon the sensitivity of the organism to the drug, the nature and extent of the infection and the clinical response of the patient. One to two grams daily, in divided doses every four to six hours, is the present recommendation. Treatment should be kept up for five to seven days. The effect of streptomycin is increased in alkaline urine. Except where urea splitting organisms are present, alkalization should be carried out.[10] Oral administration is of no value in urinary infections. While streptomycin is not destroyed by the gastric juice or intestinal secretions, there is practically no absorption through the intestinal tract.[31]

The development of resistance by bacteria to the action of streptomycin is of great practical importance. The mechanism is not known but its effect has been observed by numerous workers. It is the primary cause of failure in therapy. This proves the importance of giving, from the onset of treatment, adequate doses of the drug in order to control the infection as rapidly as possible before resistance develops. Bacteria which exhibit this tendency to resistance are not likely to lose it in subsequent treatment.[19]

The toxicity of streptomycin is greater than that of penicillin. Where therapy is of relatively short duration, the toxic manifestations which often accompany prolonged administration of large doses are rarely encountered. The milder reactions consist of elevation of temperature, arthralgia and skin rashes. While these may be due to individual sensitivity of the patient, there is much evidence that some of them result from a histamine-like reaction due to impurities in the drug. The newer products have shown less of this type of impurity. As a rule these milder reactions do not necessitate withdrawal.

The more serious complications consist of neurotoxic signs such as vertigo, locomotor disturbances, tinnitus and, more rarely, deafness, apparently the result of a selective toxic action on the eighth cranial nerve. In cases where streptomycin is to be given in high doses for a prolonged period, the patient should be warned of the possible occurrence of such symptoms. If such disturbances continue, the drug should be discontinued.[23]

The value of streptomycin in urinary tract infections has been established. In a survey for the National Research Council, Keefer and his group[24] reported a relatively high recovery rate in cases in which penicillin or the sulfonamides had failed. Uniformly poor results have been reported in patients with neurogenic bladders. This has been attributed to the presence of catheters, suprapubic fistulae, calculi and residual urine.[18] Such cases have always been refractory to treatment; mixed infections are usual.

Streptomycin has been found of value in the treatment of tuberculosis.[29] Some series have been reported on its use in urinary tract involvement.[16] The symptomatic improvement of lower urinary tract lesions is impressive and a few instances of disappearance of tubercle bacilli from the urine have been observed. There was a large percentage of recurrence of the infection. This indicates that the tubercle bacillus rapidly becomes resistant to the drug.[15] Where streptomycin is used in urinary tuberculosis, it will probably be necessary to continue the drug for several months. It is not necessary to use the large toxic doses, as ½ gm. of streptomycin once daily seems sufficient to stop proliferation of sensitive tubercle bacilli.

It is still too early to evaluate these results. The combination of streptomycin with promin, one of the newer sulfonamides, is being used in some centers. This may prove helpful in bilateral involvement. At present, the treatment of unilateral renal tuberculosis is surgical.[7]

CONCLUSIONS

The use of the newer chemotherapeutic agents has greatly increased effectiveness in the treatment of renal infections but it has not simplified the process. Proper use of these drugs places new responsibilities upon the physician. He must know what organism is causing the infection and which drug will combat it. He must have an accurate knowledge of the dynamics of the urinary tract. He must be alert to the signs of toxicity. He must be mindful of the possibility of drug resistance. He must keep his patient under constant supervision

and be prepared to vary the treatment with changes in clinical and bacteriological findings. These added responsibilities will be rewarded with vastly superior clinical results.

The ideal urinary antiseptic is yet to be discovered. The tremendous advance made during the past decade has given fresh impetus to the scientific investigator. Clinical medicine must keep step with this progress.

727 West Seventh Street.

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The Electrocardiogram in Rheumatic Fever

Julius Kahn, M.D., Edward Shapiro, M.D., Maurice L. Lipkis, M.D., *Beverly Hills*

In a consideration of the electrocardiographic changes in rheumatic fever, it must be kept in mind that the changes found are not specific for this disease alone. They are resultant from changes in the structure and endogenous chemistry of the heart, such as could be brought about by a variety of etiological factors, and hence, the individual electrocardiographic changes of rheumatic fever are seen in various diseased states. However, in few disease entities is the heart, and hence the electrocardiogram, so frequently involved as in the disease under discussion.

USUAL ELECTROCARDIOGRAPHIC FINDINGS IN ACUTE RHEUMATIC FEVER

In active rheumatic fever each segment of the electrocardiogram may be altered and the rhythm may also be disturbed.

By far, the most common change is an increase in PR interval. In the observations of different investigators, this change has been noted in varying proportions, from the 93.8 per cent of Rothschild, Sachs and Libman and the 84 per cent of Cohn and Swift, to the 5 per cent in the cases of Filberbaum, Griffith, Solley and Leake.[2,5,19,21] Discrepancies such as these are due to various factors. The electrocardiographic changes in rheumatic fever are often fleeting, and hence, the more frequently tracings are taken, the greater will be the likelihood of detecting abnormalities. Thus in the series of Cohn and Swift, 2,591 tracings were taken on 37 patients; in the series of Filberbaum and his coworkers[5] 9,634 readings were taken on 6,000 patients. Another reason for the variance may lie in the stage of illness of the patients observed. Positive findings are common in the active stage but disappear with the subsidence of the disease process. The patients of Cohn and Swift[2] were in an active stage of the disease. A large proportion of the cases of Filberbaum were in men who were several weeks beyond the zenith of the disease. This latter observation does not mean that changes in the PR interval must necessarily occur during the acute fulminant stage. Frequently, prolongations of this segment are observed after the fever and joint symptoms have subsided.[5,21] However, with the return to normal of all other signs of activity—tachycardia, fever, joint symptoms and blood findings—the PR interval in most cases also returns to normal. In a few cases, however, it may persist for weeks and even many months. In these latter cases, permanent damage of the conducting tissue must be suspected.

The degree of AV delay as demonstrated by the electrocardiogram may vary from findings within the range of normal, through various stages, up to complete dissociation. Dropped beats of the Wenckebach pattern may take place. Great variations in the PR interval may occur in the tracings of a given individual within a short space of time. As was previously noted, these changes are not entirely dependent on other signs of rheumatic fever. Their occurrence, however, in serial tracings, does indicate rheumatic activity.

Cohn and Swift[2] have demonstrated that, in the normal individual, prolongation of the PR interval can occur, probably as a result of vagal influence. However, these changes do not exceed 0.02 seconds. An increase of 0.04 seconds then would be indicative of a pathologic process or function. Thus, an individual whose normal PR interval measured .14 seconds could develop a measurement of .18 or .19 seconds, which, although within the limits of normal for some persons, would be for him abnormal and suggestive of myocardial disease.

QRST CHANGES

The frequency of changes in the QRST or ventricular portion of the electrocardiogram in rheumatic fever, as is the case with PR interval changes, will also vary with the acuteness of the disease process. Thus, in the Rothschild, Sachs and Libman[21] series, QRST changes were noted in 80 per cent of the cases. In a recent series of acute cases observed in an army hospital by Wendkos and Noll,[25] 11 per cent of the patients exhibited changes which were judged significant, while among the 6,000 patients of the Filberbaum study, 7 per cent had changes in the ventricular portion of the electrocardiogram. In the QRS segment deviations from normal varied from the 53 per cent figure of the Libman[21] study to 7 per cent in the study of Filberbaum and his associates. It is our impression that, in part, the higher proportion of abnormalities in the earlier studies such as those of Cohn and Swift[2] and of Rothschild, Sachs and Libman,[21] is due to the inclusion of grades of widening of this complex and of axis deviations which today, in the light of recent studies on large groups of normal healthy individuals, would not be considered significant.[3,6,23,24] Nevertheless, gross widening of this segment beyond the normal of the individual under observation would be considered important, as would distinct shifting of the electrical axis. Absence of R_{CF4} or R_{V4} is another finding generally indicative of myocardial involvement.

Elevation or depression of the ST portion of the electrocardiogram has been reported to vary from

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the 45 per cent figure of Rothschild, Sachs and Libman to the 1.23 per cent of Filberbaum and his associates. The latter authors felt that unless the ST changes were marked or variable, or else associated with other changes in the electrocardiogram, they were in most instances not of great significance. However, when the ST change was marked, or changed from time to time in serial observations, or when it was associated with changes in other segments of the electrocardiogram, especially of the T portion, then this abnormality became definitely important.

T wave changes, namely depression, diphasic character, or inversion, except when occurring as an isolated finding in the third lead, are in general an indication of myocardial or pericardial change. The combination of T wave changes in leads I and II, II and III, I and IV and, as is frequently the case with pericarditis, in all leads, indicates cardiac damage. The association of T changes with ST changes, especially the combination of an elevated ST with a negative T, is apt to be important.

So far as the frequency of occurrence is concerned, we find the same widespread variance in T wave changes as with changes in other segments. Thus, Rothschild, Sachs and Libman[21] report an incidence of 60 per cent, while Filberbaum and his associates[5] report 2.08 per cent involvement. The figures of other observers fall between these extremes. Here the stage of the disease and the frequency of observation play a role.

DISTURBANCES OF RHYTHM

The most important arrhythmia occurring during the course of active rheumatic fever is auricular fibrillation. It occurs with less frequency in active rheumatic fever than in mitral stenosis with rheumatic activity quiescent. When present in acute or subacute rheumatic fever it is usually accompanied by heart failure and it is usually transient in character, ceasing with the subsidence of congestive failure.[29] A group of disturbances interpreted as being indicative of increased sensitivity of the A-V node were found by Filberbaum and his associates[5] in relatively high frequency. Thus, nodal extrasystole, nodal rhythm, nodal tachycardia and ventricular escape were found 25 times in 6,000 patients, an incidence of 0.41 per cent.

Various changes in rhythm or in the electrocardiogram not infrequently occur, but in recent years these have not been thought to be of great significance. Thus, extrasystoles occur scarcely more frequently among patients with rheumatic fever than in normal individuals. Minor variations in the pacemaker would also fall in this category. Changes in amplitude of the P and T segments and shifts of the electrical axis have also been thought less important as indications of rheumatic fever activity.

To recapitulate at this point, the electrocardiographic changes of rheumatic fever are not specific for this disease. The change of greatest frequency is prolongation of the PR interval which may occur in varying degrees up to complete dissociation of auricle and ventricle. After the teaching of Cohn and Swift[2] an increase of over 0.02 seconds in the PR interval should be considered significant. Changes in the PR interval can occur either in the acute or subsiding stage of the disease. Only in rare cases does this change persist with quiescence. Changes in the ventricular portion of the electrocardiogram are also important. Gross changes in the QRS segment are significant as is also an absent R_4. Marked elevation or depression of the ST segment and T wave depressions are significant especially if the two are combined. All these changes are of added significance if it can be shown that they are deviations from the individual's normal tracing. Auricular fibrillation is the most significant of the arrhythmias that can occur during the course of rheumatic fever. Other disturbances of rhythm, those involving the A-V node possibly of greater importance, are not infrequently noted.

A word should here be interpolated that not all patients with rheumatic carditis, even when the disease is severe, show electrocardiographic changes, and also marked electrocardiographic changes can occur without clinical evidence of disease.

THE BASES FOR THE ELECTROCARDIOGRAPHIC CHANGES OF RHEUMATIC FEVER

The widespread involvement of the blood vessels of the heart in rheumatic fever is well recognized. Karsner and Bayless[10] demonstrated involvement of the coronary arteries or their branches in each of 56 autopsies on patients afflicted with rheumatic fever. These authors cite corroborative evidence in the works of many investigators. Myocardial involvement, secondary to this vascular change is to be anticipated and has been repeatedly described. Electrocardiographic changes resultant from this pathological change are also to be expected, and are found more frequently in rheumatic fever than in any other common febrile disease. Pericarditis of rheumatic origin also contributes its quota to the altered electrocardiographic patterns. Cardiac enlargement secondary to myocarditis may or may not lead to alteration of the electrical axis. When secondary to valvular defect the resultant chamber enlargement determines the degree of axis shift, if any results.

The origin of the prolongation of the AV conduction time has received considerable attention through the years. Cohn and Swift,[2] in 1924, recorded some slight variation in normal individuals from day to day, and with the phases of respiration. As was previously noted, these changes did not exceed 0.02 seconds. A possible vagal origin was suggested. In 1937, Bruenn[1] reported 22 patients suffering with active rheumatic fever and manifesting prolonged AV conduction time, in 18 of whom the intravenous injection of 1.5 to 3 mg. of atropine sulphate eliminated this defect. In two of these patients, marked emotional stress temporarily re-

duced the conduction delay, thus suggesting a sympathicotonic influence. Epinephrine administration was then found to duplicate these results on both the rheumatic fever patients and the controls. Bruenn concluded that in rheumatic fever the delay in AV conduction was ascribed, at least in part, to increased vagal tone, and he suggested a focus of irritability in the medulla as its source. Shortly thereafter, Keith,[11] in a well controlled study, repeated Bruenn's findings. Keith felt that the origin of the accentuated vagal effect was peripheral and was probably linked up chemically with the inflammatory process in the heart. More recently, Gubner, Szucs and Ungerleider[8] also suggested peripheral involvement as the source of the increased vagal or cholinergic influence, postulating a decreased suppression of cholinesterase, in turn, a result of the increased acidity of inflamed heart muscle. The absence of a general systemic vagotonic effect is offered as additional evidence of peripheral rather than central origin of this finding.

SPECIAL TECHNIQUES IN THE DETECTION OF ELECTROCARDIOGRAPHIC CHANGES IN RHEUMATIC FEVER

Findings such as those noted have stimulated some interesting attempts to utilize this apparent increased vagal tone in this disease to diagnose cardiac involvement. Gubner, Szucs and Ungerleider[8] found rheumatic fever patients with normal AV conduction time in whom they were able to distinctly prolong the PR interval by pressure on the right or left carotid sinus. This effect was best obtained with the patient in the upright position. The likelihood of a positive response was greater when the left side was stimulated. A preliminary subcutaneous injection of 0.5 mg. of prostigmine augmented the response to carotid sinus pressure. These effects were not obtained on a group of controls.

An analogous procedure, utilizing injections of ergotamine tartrate, which enhances vagal action, has been demonstrated by Wendkos.[26]

Another procedure, already mentioned but deserving reemphasis, for the detection of cardiac involvement in rheumatic fever, is the taking of frequently repeated electrocardiograms. By this practice, the normal for the individual is established and transient changes are more readily observed.

The use of multiple precordial leads in rheumatic fever may be expected to increase the proportion of positive findings in this disease as it has in other types of cardiac involvement. Wendkos and Zierler[27] have recently presented several cases illustrating this point.

THE ELECTROCARDIOGRAM IN THE DIAGNOSIS OF RHEUMATIC FEVER

As has already been pointed out, the electrocardiographic changes in rheumatic fever are not specific for this disease, but can be duplicated by a variety of diseases and circumstances. Hence, although the heart is more commonly involved in rheumatic fever than in any other common febrile disturbance, a certain amount of caution is necessary in drawing conclusions from electrocardiographic changes.

Some of the circumstances and diseases other than rheumatic fever in which electrocardiographic changes have been demonstrated and which might at times create difficulties in diagnosis will be considered.

In recent studies on large groups of healthy young people, gross deviations from accepted normal values in the electrocardiogram were demonstrated.[6,23] Graybiel and his associates[6] found the PR interval between 0.21 and 0.28 seconds in 16 of 1,000 healthy young aviators, an incidence of 1.6 per cent. Special cardiologic study in these variants failed to yield evidence of disease. In this same study, the authors found 27 men with a QRS of 0.11 seconds instead of below the accepted upper limit of normal 0.10 seconds, and 11 with a QRS of 0.12 seconds or higher.

Displacement of the ST segment more than 1 mm. above or below the base line, considered the normal range, occurred in a sizable group; and inversion of the T wave in other than the third limb lead occurred three times.

Variations from what is considered the normal electrocardiograms have been described in healthy individuals with change of posture.[14] Intense emotional stress has produced distinct electrocardiographic alterations.[12,13,28] Smoking, for a short time after its performance, has been shown to cause definite, though transient, electrocardiographic changes.[7,20]

Drugs, such as digitalis, quinine and atabrine, which alter the electrocardiogram might at times create confusion.

Some of the febrile diseases which may at times resemble certain expressions of the rheumatic fever state and which have at times been found to be accompanied by electrocardiographic changes are influenza,[9] atypical pneumonia,[17] tuberculosis,[15] typhoid fever,[18] infectious mononucleosis,[4] and disseminated lupus erythematosus.[15] Some of the arthritides are, in some circumstances, most difficult to distinguish from rheumatic fever. For example, rheumatoid arthritis and gonorrheal arthritis are not infrequently associated with electrocardiographic defects.[15,16]

The aforementioned entities, which may, by their clinical and electrocardiographic aspects, simulate phases of the rheumatic fever state, and thus possibly make diagnosis difficult, seem like a formidable array. Nevertheless, the practitioner may be comforted by the fact that in most cases of rheumatic fever the diagnosis is readily apparent on clinical grounds, and that the electrocardiogram is altered so much more frequently in rheumatic fever than in most diseases which might simulate it, that the presence of a distinct change in the electrocardiogram may be looked upon as a point indicative of this disease.

SUMMARY

The important electrocardiographic changes in rheumatic fever have been enumerated.

Some of the mechanisms of their production have been discussed.

A few procedures to increase the value of the electrocardiogram in the diagnosis and observation of rheumatic fever have been touched upon.

Some of the diagnostic problems related to the use of the electrocardiograph in rheumatic fever have been mentioned.

123 North San Vicente Boulevard.

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CASE REPORTS

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Aphthous Oral and Genital Ulcers With Conjunctivitis (Behcet's Triple Symptom Complex)

LAWRENCE M. NELSON, M.D., AND H. I. BURTNESS, M.D.
Santa Barbara

ALTHOUGH others had previously reported similar cases, Behcet[1] is generally credited with first recognizing the interrelationship of the symptoms comprising what he termed the triple symptom complex. Curth[3] has brought the subject up to date in an excellent article published in 1946. The following case is reported because of the complete investigation which the patient received in three institutions and because of the apparent rarity of the condition.

A 17-year-old male, native of California, was admitted to Santa Barbara Cottage Hospital January 15, 1947. He developed "canker sores" in 1945. These lesions became progressively more severe and were quite painful. He was unaware of any blisters at any time. He had been free of lesions at intervals but in the free intervals had had a redness of the throat. In an auto accident in the fall of 1945 he received a laceration of the right eye and of the forehead and nose. He was given sulfonamides and hyperpyrexia at that time and was free of oral lesions for some time thereafter. However, the lesions reappeared and progressed. He was twice hospitalized elsewhere* for this condition and was very thoroughly investigated. In August, 1946, perianal lesions appeared, and in September, 1946, scrotal lesions appeared. In mid-September, an abscess developed about a foreign body in the nose, and the patient was hospitalized, the abscess drained and penicillin administered. The scrotal lesions became much worse during this time, and he was confined to bed most of the time from then until he came under our observation.

The patient had had the usual diseases of childhood. He had lesions described by his father as blisters around the mouth, beginning when the patient was nine months of age and persisting for an unspecified period. At fifteen months of age he developed asthma, which persisted into his sixteenth year. Tonsillectomy was performed at age five. An appendectomy was followed by phlebitis at age 12. At age 12 he also suffered from a severe sore throat which lasted for three weeks. He was run over by a tractor with resultant injury to the shoulder girdle at age 13, suffered a severe burn of the back at age 14, and had an injury of the nose, followed by infection, at age 15. The infection was treated with penicillin.

The patient has been hospitalized five times at the Cottage Hospital and once at a Mid-west clinic† since he came under our observation. When first seen January 15, 1947, he weighed 110 pounds, a loss of 27 pounds from his best weight. He presented partial baldness of the borders of the tongue. On the right lower lip was a heavily crusted ulcer. The nasopharynx was partially denuded and whitish as though there was a great deal of underlying scar tissue. At the base of the penis and extending on down to the scrotum and the right perineum was a heavily crusted, foul smelling, deep ulcer, with rolled borders. The base was covered with thick creamy pus. Aside from the laceration of the right eye, the eyes appeared normal. The temperature was normal upon admission and remained so throughout all the hospitalization, except when fever was induced.



Extent of ulceration during most recent hospitalization.

While the patient has been under our observation the lesions have been present intermittently and have become increasingly severe. There has been some hemorrhage from the lesions at times.

Injection of the left cornea was noted in January of 1947, at which time repeated questioning brought out that there had been mild injection of the cornea at intervals for some time. He continued to have occasional corneal injection. In September, 1947, the right lid margins became thickened and crusted. Vision had not been impaired at any time (other than from the old injury to the right eye). Late in 1947 the patient first noted photophobia. In May, 1947, he noted a blister over the left deltoid. This blister broke, resulting in a typical ulcer. He also developed pustules followed by ulcers at the sites of therapeutic smallpox injections and some of the skin tests in late 1947. About the same time he noted blisters on the toes. These blisters healed without destroying the skin, and none were present when he was under our direct observation. Eye examination in March, 1947, showed the left retina to be essentially

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*Robert C. McNaught, M.D., provided a resume of the patient's record at Stanford University Hospital.

†Robert R. Kierland, M.D., provided a resume of the patient's record at The Mayo Clinic.

normal. The conjunctiva was pale and somewhat edematous at the fornices. The right eye could not be examined because of the old injury. He was followed during December, 1947, by an ophthalmologist. At no time was iritis found. The left optic disc arterioles and venules were normal in color and contour. There was one small, pinhead-sized, dull black pigment speck adjacent to the inferior temporal vessels 6 disc diameters out from the disc. Elsewhere about this area and in other areas the extreme periphery was somewhat more pigmented than one would expect in this type of fundus; however, this pigmentation was not a pattern which could be identified as any pathological process at that time.

Laboratory: The reports from all three institutions in which this patient was hospitalized were made available to us and will be presented together. Results of histoplasmin and coccidioidin tests were negative in June, 1946, and September, 1947. Tuberculin test 1-10,000 was negative as was the Frei test. Moderate anemia was usually present 10.5-13 gm. (64 per cent-84 per cent). The patient often had a relative neutropenia (as low as 51 per cent) with an occasional moderate leukocytosis up to 12,500 per cubic millimeter. Serologic tests for syphilis were negative. Roentgen examinations of the chest revealed no abnormalities. Blood culture was negative. Cultures from the lesions showed various organisms at various times. Staphylococci and green-producing streptococci as well as proteus vulgaris were found. At one time coagulase-positive, pigment-producing hemolytic staphylococcus aureus was found in the eye and in the nasopharynx. Fungi and tubercle bacilli could not be cultured. Stool culture showed no members of the typhoid or paratyphoid group. Undulant fever agglutinations were positive 1:20 through 1:320 upon one occasion but were subsequently negative. There was no reaction when brucellin was administered intramuscularly. Repeated urinalyses were normal except for a few hyaline and granular casts upon one occasion and a slight trace of albumin upon another occasion. Darkfield examinations of the exudate from the lesions showed no spirochetes. The seventeen ketosteroids were reported as 5.2 mg. per 24 hours. Blood, biopsy specimens, curettings from the ulcer base, stool specimens, smears from the ulcers, and paraffin sections were examined for virus‡ The sections were stained with eosin-methylene-blue. The smears were stained with Giemsa, Macchiavello's stain and methylene blue. None of the material examined showed any evidence of inclusion bodies, either cystoplasmic or intranuclear. No immune bodies for herpes simplex were demonstrated in the blood serum by a simple neutralization test in mice.

The biopsy specimen and some of the whole blood were inoculated intracerebrally into six-day unweaned mice. Some of the animals were sacrificed at the end of one week, the rest at the end of two weeks, and material passed on to another set of six-day mice. These were observed for one month. Adult mice were also inoculated with biopsy material and carried for three passages. The curettings and stool specimens were inoculated into young rabbits by scarifying the corneas. Some of the biopsy material was inoculated to the chorio-allantoic membrane of ten-day chick embryos but was not carried beyond the second passage because of difficulty with bacterial contamination which persisted in spite of the use of penicillin and streptomycin. Biopsy material (which had been stored in dry ice for two weeks) was inoculated into hamsters. In all respects, the specimens were completely negative for virus material that could be transmitted to laboratory animals.

‡Virus investigations were performed by Peter L. Beal, M.D.

TREATMENT

Local therapy, including tyrothricin, permanganate, and dilute acetic acid was ineffectual. The lesions progressed in spite of systemic treatment with streptomycin, penicillin, blood transfusion, the sulfonamides, folic acid, protein hydrolysate and vitamin supplements. The patient was also subjected to numerous bouts of hyperpyrexia by means of triple typhoid vaccine and the Kettering hypertherm. Benadryl, crude liver extract, testosterone, and repeated intracutaneous injections of smallpox vaccine were also tried. Exacerbations and relapses occurred in spite of all treatment, although it was our opinion that, for a considerable time, the severity and the duration of the attacks were materially lessened by the use of triple typhoid hyperpyrexia. Such therapy was without effect, however. during the most recent hospitalization.

DISCUSSION

In the case under consideration, the following conditions were considered in differential diagnosis:

1. Erythema multiforme of the ectodermosis erosive pluriorificialis type. This condition is primarily a vesicular and bullous disease which usually has an acute onset with fever and constitutional symptoms. It usually runs its course in from three to six weeks. Relapses occur but are not the rule.

2. Pemphigus: The age of the patient and the lack of true bullae ruled against this condition. Pemphigus vulgaris does not involve the eye and no type of pemphigus results in such ulcers as this patient presents.

3. Dermatitis medicamentosa: The medication which this patient takes has been known and followed for a prolonged period of time.

4. Aphthous fever: (foot and mouth disease). This condition, which is self-limiting and primarily a vesicular disease, was ruled out by the history, as well as by the recurrent attacks which the patient suffered.

5. Periadenitis mucosa necrotica recurrens (ulcus neuroticum mucosae oris). This disorder is described as beginning with smooth, red, hard nodules which slough out a solid, mummified plug leaving a crateriform depression which heals in five to eight days. Fordyce[5] has seen this condition on the vaginal mucosa. It may be that some of the cases described under the above title belong to the group known as triple symptom complex or vice versa, but the patient under consideration did not have primary lesions as hard nodules, and plugs of tissue were not sloughed. Also. the lesions became much larger than those described under the above title and persisted much longer.

6. Aphthous ulcers: Touraine[7] has suggested that aphthous ulcers, triple symptom complex, periadenitis mucosa necrotica recurrens, ulcus vulvae acutum, and several similar conditions be classed as members of one group, the aphthoses. On a clinical basis alone, it would be impossible to differentiate the lesions of the less severe cases of triple symptom complex from those of the more severe cases of aphthous ulcers. The lesions presented by this patient were more severe than those usually termed aphthous ulcers, but there was no way of proving that he did not have aphthous ulcers. Laboratory tests did not clarify the diagnosis.

7. Ulcus vulvae acutum: Ephraim[4] states that this condition has been seen on the scrotum, root of the penis and on the buttocks. What has been said about aphthous ulcers also applies to this condition. Oral lesions sometimes accompany ulcus vulvae acutum. The presence of bacillus crassus in the lesions would favor a diagnosis of ulcus vul-

vae acutum, but there is reasonable doubt that these organisms have any causal relationship to the condition. These organisms were present in Curth's second case.[3]

After considering the above conditions, this patient was thought to have the triple symptom complex as described by Behcet[1] because of the insidious onset, the type and location of the lesions, the recalcitrance to all forms of therapy, the conjunctivitis, and the formation of pustules at the sites of skin abrasions from intracutaneous and subcutaneous injections. Iritis leading eventually to hypopion is the usually described eye condition associated with triple symptom complex. The diagnosis in the case presented might be challenged since only conjunctivitis was present. However, Behcet[2] points out that eye lesions may not be present and Franceschetti and his coworkers[6] state that the first sign of eye involvement may be photophobia and irritation of the ball, and that iritis and hypopion may develop only very late in the disease. Moreover, the skin manifestations are usually, but not always, present for some time before any eye symptoms appear. Since iritis is a manifestation of disease elsewhere in the body, it is not surprising that it sometimes develops in association with these chronic recurrent ulcers.

The ophthalmologist who observed the patient suggested that the eye picture in the case being presented might be due to contamination from the oral and genital lesions. That theory was partially borne out by the finding of identical pigment-producing, coagulase-positive staphylococci in the nasopharynx and in the eye. However, these organisms were found in the eye but once. Only time will tell what picture the uninjured eye will eventually develop.

The extensive laboratory investigations to which this patient was subjected revealed nothing relative to the cause. The low seventeen ketosteroids had not been previously found, but therapy in the form of testosterone did not result in any improvement; this finding probably had nothing to do with the skin picture. The investigations of one set of samples for viruses were negative as were similar investigations reported by Curth.[3] The elementary bodies described by Behcet[2] were not found. Aside from streptomycin, testosterone, and tyrothricin, all therapy used on our patient had been tried previously on patients with this condition.

SUMMARY

The case of a 17-year-old white male who has recurrent painful ulcers of the oral cavity and genitalia, as well as recurrent conjunctivitis, is presented. This patient is thought to have the triple symptom complex described by Behcet. No cause was found for the condition and no treatment has appreciably influenced the course of the disease.

1520 Chapala Street.

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Carcinoid of the Appendix, Simulating Closely Primary Carcinoma of the Appendix

MELFORD B. JORGENSEN, M.D., *Los Gatos*

THIS is the report of a case of carcinoid of the appendix that closely simulated primary carcinoma of the appendix. This case was somewhat unusual in that there was a history typical of recurrent attacks of acute appendicitis of ten years' duration, and some of the attacks had been quite severe. One month before the patient was operated on, she had a moderately severe attack. She wanted to postpone operation, if possible, for a month or two, when she could have a uterine suspension, ovarian cystectomy, and conization of the cervix, as well as the appendectomy.

Both Foot and Boyd intimate that carcinoid tumors are usually found at operations for other conditions than disease of the appendix, or at necropsy. Carcinoid tumor of the appendix is found in 0.3 to 0.4 per cent of appendices removed surgically, according to Boyd. This condition has been described in the literature as primary carcinoma of the appendix, and the case here reported was originally thought to be one of primary carcinoma. Five pathologists, however, were of the opinion that the tumor was carcinoid.

True adenocarcinoma of the appendix is extremely rare. Boyd states the histological picture suggests carcinoma, while the clinical course is usually that of a benign lesion. In 90 per cent of the cases the lesion is situated near the tip of the appendix. The appendix is usually not elongated, but may be broader than usual, and firm. A membrane may be present on the surface. Cross-section reveals a yellow ring which encircles the appendix and appears to be situated in the submucous coat. This is due to a lipoid material. Microscopically the tumor consists of spheroidal cells, arranged in very definite groups or masses suggestive of a carcinoma, and although never showing a true gland-like arrangement, sometimes the cells may be grouped around a rather atypical and irregular lumen, as they were in this case. Although usually confined to the mucous and submucous coats, the cells may penetrate the muscularis, and even the subserous coat, as they did in this case.

Carcinoid tumors may be found in any part of the gastrointestinal tract, although most frequently in the small intestine, where they are often multiple. In the appendix they are always single.

CASE REPORT

The patient, a 37-year-old white married woman, was first observed February 3, 1947, because of steady, dull pain of three days' duration in the right lower quadrant of the abdomen. There had been some nausea but no vomiting. Bowel movements were normal. Past history revealed recurrent episodes of similar distress over a period of ten years. The patient had also had considerable dysmenorrhea since puberty, and had had considerable low back pain in the preceding five years. There was a persistent vaginal discharge which had begun three years previously. The patient was well developed and well nourished and was not acutely ill. The temperature was 99.6° F., the pulse rate 86, and the blood pressure 120 mm. of mercury systolic and 80 mm. diastolic. Heart and lungs were normal. The abdomen was flat with slight rigidity and moderate tenderness in the right lower quadrant and there was slight rebound tenderness. Rectal examination disclosed no abnormality. Upon examination of the pelvis the cervix was found to be moderately eroded and everted, and the uterus was retroverted. There was a cyst measuring 3 x 4 cm. in the left ovary, which was tender. The right adnexial region was moderately tender.

Examination of the blood showed hemoglobin 88 per cent (15 gm. per 100 cc.). Erythrocytes numbered 4.3 million and leukocytes 10,300 with normal distribution of polymorphonuclear cells, lymphocytes, stabs, segmented cells and monocytes. A Wassermann test of the blood was negative. Urinalysis was normal.

The diagnosis of recurrent appendicitis was made and the patient was observed closely. On February 26, 1947, she was operated upon. The appendix, which was elongated and moderately broad, lay retrocecal and was completely bound down to the posterior surface of the cecum by dense adhesions. It was surrounded by moderate inflammatory reaction. The uterus was retroverted and there was moderate relaxation of the supporting ligaments. A cyst measuring 3 x 4 x 3 cm. was found in the left ovary. The cervix was moderately eroded and everted.

Operation consisted of uterine suspension, ovarian cystectomy, appendectomy, and conization of the cervix.

Pathological Report: The appendix was 5 cm. in length and 0.7 cm. in thickness at each end. In the distal third there was a localized fusiform swelling involving the entire appendiceal wall and measuring 1.2 cm. in thickness. At the swelling the wall was yellow, the lumen being obliterated by firm, yellow-white mucoid-appearing material. Microscopic examination of sections showed the serosal surface to be intact. It was covered with flattened spindle-shaped cells. The subserosal connective tissue was sparse but in some areas contained dilated blood vessels engorged with blood. Longitudinal and circular muscular coats were well defined, but the mucosa was totally altered by the presence of a tumor made up of large, rounded islands of cells. Between these islands were elongated, irregularly shaped strands and columns of tumor cells packed fairly closely together and infiltrating the stroma without limits. These cells had invaded the muscular walls in many places, and in one area were present in the subserosal connective tissue adjacent to the serosa. Wherever seen the cells were similar in character, being fairly small and round, with scanty cytoplasm and round to ovoid nuclei which were dark staining, with discrete nuclear membranes and dusty particles of chromatin material dispersed throughout the nucleus. Some contained fairly well defined, slightly irregularly outlined nucleoli in their central portions. Mitotic figures were not observed.

Diagnosis: Argentaffinoma (carcinoid), appendix.

The patient made a very satisfactory recovery and was dismissed from the hospital on the sixth postoperative day. Examined every two months since leaving the hospital, she has had no complaints other than of an occasional pain in the right lower quadrant, where slight tenderness has persisted. Otherwise the abdomen appears to be normal.

COMMENT

These rare tumors of the appendix are of interest to the surgeon because of the differential diagnosis, and because they may be the source of a metastatic lesion, the treatment of which may be somewhat of a problem, with necessity for fairly close observation of the patient for many years. The great majority of the patients are completely cured by removal of the carcinoid tumor.

As a rule a carcinoid tumor behaves in a benign manner, although it may infiltrate the wall of the appendix. It may, however, metastasize to the regional lymph nodes and also to the liver. Metastasis is more likely to occur from a carcinoid tumor in the small intestine than from one arising in the appendix. Metastases are, however, always slow to occur and slow to cause termination. Boyd states metastatic lesions have been found as late as 20 years after a carcinoid tumor was removed.

Many of the cells of a carcinoid tumor contain granules which stain black with silver salts (argentaffin) and yellow with chromium salts (chromaffin). A relationship exists between carcinoid tumors and argentaffin-cell neuromas. Apparently the paraganglionic cells in the plexus of Meissner and Auerback have something to do with the origin of the tumor. Some believe that this may be the origin of the so-called "neurogenic appendix."

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Disseminated Coccidioidomycosis: Isolation of Causative Organism from the Urine

Mervin J. Goldman, M.D., and Eli Movitt, M.D.,
Oakland

In the case of disseminated coccidioidomycosis which is reported here, a very unusual feature occurred which, to the best knowledge of the authors, has never been reported previously.

CASE REPORT

A 27-year-old negro male was admitted to the Oakland Veterans Administration Hospital January 28, 1947. The patient was born and reared in Paris, Texas. He served in the Army from February, 1942, to August, 1944, most of the time in Louisiana. He had no overseas service. The past history was negative except for syphilis contracted in 1942 and treated for six months with mapharsen and bismuth with subsequent negative results of blood and spinal fluid examinations. A review of Army medical records revealed repeatedly negative chest roentgenograms. Upon release from the military service the patient came to Oakland, California. In the latter part of 1946 he moved to Madera, California (located in the San Joaquin Valley), where he worked as a crop picker up to the time of the present illness which began December 1, 1946, with chills, fever, cough, and right chest pain. He was treated at a local hospital for right lower lobe pneumonia with penicillin and was discharged January 1, 1947. He continued to feel weak, and had a cough productive of small amounts of green sputum. On admission to the Oakland Veterans Administration Hospital the temperature was 102° F., pulse rate 110, respirations 24 per minute and blood pressure 100 mm. of mercury systolic, 60 mm. diastolic. The patient appeared acutely ill and showed evidence of considerable weight loss (height 73 inches, present weight 135 pounds, average weight 152 pounds). No palpable lymph nodes were present. The lungs were clear to percussion and auscultation and the remainder of the physical examination was negative. The routine and follow-up laboratory data are shown in Table 1. The Kahn test of the blood was negative. The blood urea nitrogen was 12 mg. per 100 cc. A roentgenogram of the chest, taken on admission, was reported as follows: "The cardiac shadow appears normal. Both lung roots are moderately prominent and there are some faint exudations in the right mid-lung field with an area 1 cm. in diameter which may represent a cavity. On

From the Medical Service, Oakland Veterans' Hospital.

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TABLE 1.—*Results of Sputum, Urine and Blood Examinations for Coccidioides*

Date	RBC (Million)	Hgb. (Gm.)	WBC	Sed. Rate mm./hour	Urine Sediment (cells/ h.p.f.)	Urine Culture	Sputum	Tbl. Skin Test	Coccidioides Skin Test	Coccidioides Compl. Fixation	Blood Culture
Jan. 28	3.65	10.9	9,200	119	1- 3 RBC		Neg.				
Feb. 1					8-10 RBC		Neg.				
Feb. 3							Neg.	1:1000 Neg.	1:1000 Neg.		
Feb. 10	3.6	10.6	13,600				Neg.				
Feb. 14	2.85	9.4	8,600				Neg.				Neg.
Feb. 22									1:100 Neg.		
Feb. 24										+++++1:128 +1:256†	
Mar. 3							+C. immitis				
Mar. 13									1:10 Neg.		
Mar. 14	2.65	8.6	24,600		Loaded RBC	+C. immitis*					
Mar. 17									Undil. Neg.		
Mar. 21											+C. immitis

*Positive cultures both at Oakland Veterans Administration Hospital and at Stanford University Laboratory.
†Facilities of the coccidioidomycosis study, Commission on Acute Respiratory Diseases, Army Epidemiological Board at Stanford Medical School.

lateral projection these are seen to lie posteriorly in the upper portion of the right lower lobe." Subsequent roentgenograms of the chest on February 12 and February 24 showed no essential change.

The patient had a temperature ranging daily from 99° F. to 104° F. during the entire period of hospitalization.

On February 17 a firm and non-tender small lymph node was noted at the angle of the right mandible. This was removed for biopsy and the pathological report was as follows: "The specimen consists of a firm, irregular mass 18 x 18 x 15 mm., the outer surface of which has numerous connective tissue tags and small fat lobules. The cut surface shows considerable variation in configuration, some areas being firm, white, and semi-translucent and others opaque and hemorrhagic. Microscopically, the lymph node contains numerous localized areas of granulomatous structure in which there is moderate central necrosis, an outer zone of lymphoid tissue, and an intermediate zone of increased epithelioid formation. Among the latter there are numerous giant cells. Scattered throughout the granulomata there are numerous large double-walled structures containing numerous endospores. In addition there are many small isolated endospores characteristic of Coccidioides."

Results of sputum, urine, and blood examinations for Coccidioides are shown in Table 1. On March 4 the patient developed tenderness over the mid-sternal region. Enlarged lymph nodes appeared in the right axilla. By March 10 a definitely fluctuant mass had developed in the mid-sternum opposite the third rib. However, roentgenograms of the sternum taken at this time were normal. X-ray films of the thoracic and lumbar segments of the spine, knees, ankles, and abdomen, were all reported as negative. As no specific treatment for disseminated coccidioidomycosis is known, vaccine treatment was attempted although little hope was held for benefit. The patient also received repeated blood transfusions, but the course was progressively downhill and he died March 22, 1947.

POSTMORTEM EXAMINATION

The body was that of an undernourished, slender, negro male, measuring 6 feet 3 inches in length, and estimated to weigh approximately 100 pounds. There was a soft fluctuant mass just below the xiphoid, which, on palpation, had some bony crepitation. There was a second small fluctuant mass over the xiphoid process. Each was approximately 4 cm. in diameter. There was considerable wasting of the soft tissues.

Subcutaneous fat was negligible. The lower border of the liver was 4 cm. below the costal margin. The two small fluctuant masses on the sternum were found to be abscesses filled with thick, green, purulent exudate. Smears showed typical Coccidioides spherules. In each instance the bone was eroded. The upper lesion had completely destroyed the bone on both sides of the sternum, but had not perforated the soft tissues on either side. The lower lesion involved only the anterior table of the sternal structure.

Heart: The heart weighed 250 gm. A few small, pinpoint, white tubercles were seen through the pericardial surface. Similar depositions were observed in the myocardium and shining through the endocardium. These were minute and sparse. The muscle was pale but firm.

The right lung weighed 1,500 gm., the left 1,250 gm. The pleural surfaces were smooth, but shining through the pleura on either side were innumerable small white tubercles. The tissue, the consistency of liver, was readily cut, and innumerable small tubercles were observed on the sectioned surfaces, in all portions of the lung. There was no evidence of bronchial distribution of the tubercles, but no portion of the lung had escaped. The major bronchi did not contain exudate, and no localized abscesses were seen in the pulmonary tissues. The mediastinal lymph nodes were enlarged, particularly those in the upper portion of the mediastinum anteriorly. One of the nodes in this region was sectioned, and considerable purulent fluid exuded into

the pleural cavity. Other abscesses were found in the lymph node chain extending from the extreme upper limits of the mediastinum down to the diaphragm. The largest of these nodes was approximately 3 cm. in its greatest diameter.

Liver: The liver weighed 1950 gm. The border was rounded and the surface slightly nodular and rough, with the gross appearance of cirrhotic liver. The sectioned surface everted moderately, was resistant to cutting and appeared to be cirrhotic. In addition, there were small white, discrete tubercles scattered throughout all sectioned surfaces. The gallbladder and bile ducts appeared to be normal.

Spleen: The spleen weighed 240 gm. It was pale in color, the borders were rounded, and the tissue was moderately flabby. On the sectioned surface, as well as shining through the peritoneal surface, there were many small white tubercles. The sectioned surface everted moderately, and in several areas there were localized accumulations of thick, green pus in abscesses approximately 6 mm. in diameter.

Pancreas: The pancreas was normal in size and shape. Along the upper border of the pancreas, in the line of blood vessel drainage from the spleen toward the celiac axis, there was a group of enlarged lymph nodes, some of which contained a large amount of greenish exudate. This chain of nodes extended from the tail to the head of the pancreas.

Adrenals: The adrenals were normal in size, color, and consistency. In one adrenal in the medullary portion there was an aggregation of gray material.

Genito-Urinary Tract: The right kidney weighed 270 gm., the left 250 gm. The sectioned surface everted moderately, and was pale in color, but the line of demarcation between cortex and medulla was sharp. Studded throughout the parenchyma in both cortex and medulla were numerous small, white aggregations of material. No exudative material was found. The pelves and ureters were normal-appearing, as were the bladder, prostate, and external genitals.

Vertebral Column: There were accumulations of fluctuant masses adjacent to the bodies of the vertebrae from the seventh dorsal to the first lumbar. These were most numerous along the left side, and in four distinct areas the purulent exudate was in direct continuity with the cancellous portions of the bodies of the vertebrae. There was such an abscessed cavity on both sides of the 11th dorsal vertebrae. No evidence of extension of the exudate into the psoas muscle sheath was demonstrated.

Central Nervous System: The convolutions of the brain were normal in size and the sulci were not broad. There was no evidence of meningeal exudate or localized deposition of inflammatory material. The surface of the brain was washed and carefully examined, but no evidence of "tubercles" could be seen. The base of the brain was particularly examined, but no pathologic changes were recognized grossly.

Microscopic Examination: Microscopic examination of the lungs, heart, liver, spleen, pancreas and adjacent lymph nodes, adrenals, kidneys, subcutaneous tissue and central nervous system revealed inflammatory changes with spherules characteristic of Coccidioides.

DISCUSSION

The patient's place of residence immediately made coccidioidomycosis a consideration in diagnosis, but with the subsequent negative skin tests, adenopathy, and urinary findings, a lymphoma was considered a much more likely possibility. However, with the pathological report of the lymph node biopsy all investigative procedures were turned toward the study of coccidioidomycosis. This resulted in the finding of a positive complement-fixation and in the subsequent recovery of the organisms from the sputum, the urine, and terminally from the blood stream. It is not too uncommon to recover C. immitis in blood cultures taken within 24 hours of death in cases of disseminated coccidioidomycosis. However, it is definitely rare to find the organisms in the urine. To the best knowledge of the authors this has never been reported in the literature. The physician who examined the urine had never before isolated the fungus in the urine.*

SUMMARY

1. A case of disseminated coccidioidomycosis is presented with involvement of the lungs, lymph nodes, bone, liver, spleen, kidneys, heart, adrenals, and brain.

2. C. immitis was cultured from the sputum and urine during the course of the patient's hospitalization. A blood culture within 24 hours of death was also positive.

3. The unusual feature of this case, which is believed to be unreported previously, is the identification of C. immitis in the urine.

*C. E. Smith: Personal communication.

Urethral Diverticulum with Calculi in Women

Harry A. Zide, M.D., *Beverly Hills*

CALCULI complicating urethral diverticulum in women is rare, approximately 40 such cases having been reported. The case here reported is that of a woman aged 47 years with such a condition producing typical local symptoms and recurrent cystitis.

ETIOLOGY

The following, adapted from Johnson,[3] summarizes the present concept of etiology.

Acquired	Congenital
1. Trauma of childbirth	1. Gärtner's duct
2. Infection of urethral glands with sealing off of opening to urethra, formation of abscess and reestablishment of communication	2. Cysts formed from faulty union of primal folds
3. Instrumentation of urethra, especially deep fulguration of urethral lesions.	3. Cell rests
4. Secondary to urethral stricture	4. Wolffian duct
5. Secondary to urethral stone	5. Vaginal cysts

Johnson personally believed the majority of diverticula to be congenital in origin, either present in situ as such, or developing from congenital cysts which acquire an opening into the urethra by trauma or infection, or from infected glands of the middle third of the urethra which are there as an anomaly, according to Cabot and Shoemaker.[1] However, in regard to the last possibility, Lintgen and Herbut[5] in examination of 100 female adult urethras found glands in every case in the anterior urethra and in 65 per cent of the posterior female urethras. This would suggest that infected

From the Department of Urology, Cedars of Lebanon Hospital, Los Angeles.

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glands may be the most common cause of diverticula. Menville and Mitchell[6] agree with this theory.

The probable sequence after the diverticulum is formed has been stated by Higgins and Roen[2] to be, first, infection of the urine, then a lapse of time during which the diverticulum enlarges and urinary salts precipitate in the stagnant urine, leading to calculus formation. The possibility of calculi being passed from a kidney or the bladder and lodging in a diverticulum must be considered. In the case to be reported I believe the diverticulum formed from an infected gland and that the calculi formed within the diverticulum.

SYMPTOMS

The symptoms may be local and caused by the presence of the sac and calculi, or urinary and traceable to mid- or upper urinary tract infection.

Local symptoms usually consist of (1) a vaginal mass which may partially empty with the urethral passage of pus or urine if there is room for retained urine about the calculi, (2) urethral or perineal pain, (3) painful intercourse, and (4) possibly hematuria, especially after coitus.

Urinary symptoms result from the almost inevitable infection, and the degree depends upon the upward spread and resultant pathological changes in the urinary tract. As Johnson states, these vary from "recurrent attacks of cystitis to persistent urinary infection with exacerbations of frequency, strangury, and terminal hematuria. The presence of chills, fever and backache suggest an associated pyelonephritis."

DIAGNOSIS

A typical history of local symptoms as described would strongly suggest the presence of urethral diverticulum with or without calculi. Palpation of the urethra on vaginal examination would disclose a mass on the ventral surface of the mid-urethra which might be fluctuant until urine was expressed, then hard with possible crepitation as in the case reported.

A roentgenogram of the bladder and sub-pubic area would disclose opaque calculi. The diverticulum could be demonstrated by filling the bladder with a radio-opaque medium and having the patient void against the pressure of a finger against the meatus or obstructing the bladder neck with a bag catheter and injecting the urethra through the meatus.

Urethrocystoscopy either with the right angle lens or the foroblique lens while viewing the ventral surface of urethra with the water flowing will usually allow visualization of the orifice. (This is, by the way, a good routine practice.) A urethral catheter may then be coiled in the sac and roentgenograms taken before and after the injection of an opaque medium, both in the anterior and oblique positions. Demonstration of the size and location of the sac in relation to the base of the bladder is of aid in the surgical excision, according to Kutzmann.[4]

TREATMENT

Conservative medical treatment of urethral dilatation and urethral instillations is only palliative, since infection cannot be cured by this means.

Minor surgical procedures such as enlarging the orifice of the diverticulum with an electrical loop or knife through a cystoscope may also enable one to evacuate calculi but will not cure the original cause of their formation, the diverticulum. Incision and drainage of an acutely infected diverticulum pointing into the vagina may be necessary with later repair.

Radical surgical excision of the sac and contained calculi is the procedure of choice and usually results in cure. The procedure is first to insert a retention catheter in the bladder, which aids in visualizing the structures and in the repair of them. Then a vaginal incision is made over the sac, the vaginal mucosa dissected to each side and the sac freed by blunt or sharp dissection as may be necessary to expose the neck of the diverticulum at its junction with the urethra. The structure is then excised at this point. The urethral defect is approximated with No. 00000 chromic catgut on an atraumatic needle, the periurethral tissues with No. 00 plain catgut or fine stainless steel wire in one or two layers, and the vaginal mucosa with No. 1 chromic catgut. Antibiotics such as penicillin and streptomycin or penicillin and sulfadiazine should aid in healing by keeping the urine sterile or little infected. A vaginal pressure pack may be used for 48 hours. The catheter is left in place for seven to ten days. by which time the area is usually healed.

CASE REPORT

The patient, nullipara, aged 47 years, when first seen in January, 1948, complained of recurrent frequency and dysuria of many years' duration. In June, 1947, she noted "two lumps" in the vagina. These swellings, the patient said, enlarged intermittently, and in addition there had been generalized abdominal pains, occasional nausea and vomiting, and constipation.

Previous urologic history was that of scarlet fever at the age of ten years, followed in two weeks by generalized edema from "kidney disease." The edema cleared rapidly, the patient recalled, but after that there was always some urgency and frequency in day, voiding every one to two hours, as well as nocturia three to six times. In 1929 the patient had recurrent pain in the left flank, and a specimen taken by the catheter at that time contained pus and bacteria. There was some improvement after this, with occasional flare-ups until 1943 when symptoms increased. In 1944 a plastic operation on the left ureteropelvic juncture for congenital band obstruction was performed. This was followed by hydronephrosis and pyelonephritis for which left nephrectomy was done in January, 1946. Pyelography at that time showed the right kidney to be normal but the function was moderately decreased. The urine contained Gram-negative bacilli and one to three casts per high dry field. No albumin was present.

When examined in January, 1948, the patient was obese, 65 inches in height and weighing 195 pounds. The blood pressure was 98 mm. of mercury systolic, 68 mm. diastolic. The abdomen was diffusely tender but no rigidity or masses were noted. On the left flank there was a scar but no tenderness at the site. The urethral meatus was normal, but on the ventral surface of the mid-urethra there was a cystic swelling about 2 cm. in diameter with crepitation indicating the presence of calculi. Pressure did not evacuate fluid from the meatus.

Laboratory tests: A specimen of urine taken by catheter was cloudy, alkaline, with specific gravity of 1.018, and no albumin or sugar content. Upon microscopic examination 12 to 15 leukocytes and 4 to 5 erythrocytes per high dry field were noted, and there were many bacteria. Occasional Gram-negative bacilli, and Gram-positive cocci in clumps, were observed. A non-protein nitrogen determination of the blood done February 20, 1948, showed 27 mg. per 100 cc.

Roentgen studies: Roentgenograms of the kidney, ureters and bladder and an intravenous urogram done November 20, 1947, disclosed two small densities behind the pubic symphysis, the larger 1.5 cm. in diameter and the smaller 1 cm. (Figure 1). The upper right urinary tract, faintly visualized, was grossly normal. In a urethrogram January 22, 1948, the dye outlined a 2.5 cm. diverticulum arising from the floor of the mid-urethra and containing previously described densities. A cystogram at the same time was normal. (See Figures 2 and 3.) A gall bladder and gastro-intestinal series done in October, 1947, disclosed no abnormality.

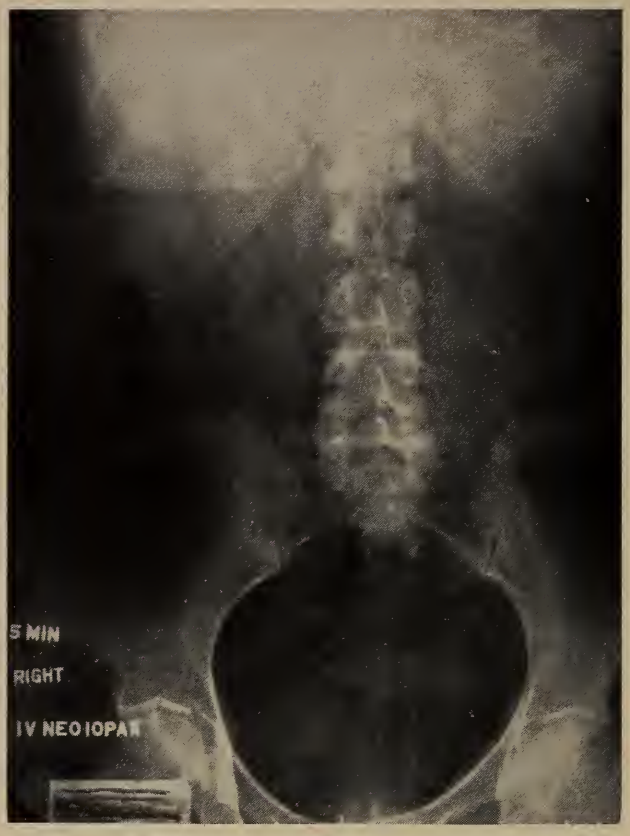


Figure 1.—Intravenous urogram, five minutes after injection, showing faintly outlined right renal pelvis with upper ureter; and two opacities just above pubis representing calculi in urethral diverticulum.

Diagnosis: 1. Diverticulum of urethra with two calculi; 2. Cystitis, chronic, mixed infection, secondary to the diverticulum; 3. Surgical absence of left kidney; 4. Hypotension, mild.

Treatment: On February 20, 1948, surgical excision of the urethral diverticulum and contained calculi was performed as described. A No. 18 (French) 5 cc. bag urethral catheter was left indwelling. A vaginal pack was inserted for pressure during the first 48 hours. Streptomycin (200 mg.) and penicillin (30,000 units) were given every three hours for three days, then every six hours for four days. Sulfadiazine, 2 gm. per day, was given subsequently.

Surgical pathology report: There was diffuse infiltration of leukocytes in the connective tissue. The mucosa was covered by transitional epithelium, with the cells considerably swollen. In the underlying stroma there was diffuse inflammatory infiltrate and in a few areas focal calcific deposits.

Two calculi, one 1.5 cm. in diameter and the other 1 cm. in diameter. They were extremely hard and the external surface was a faint greenish-gray and fairly smooth. The inner surface after splitting showed a laminated character with a whitish, softer center portion. Diagnosis: 1. Tissue consistent with diverticulum of urethra, with moderate inflammation; 2. Urethral calculi.

Postoperative course: The patient's temperature was practically normal after the operation and the urine was sterile by Gram stain to the 15th day. Despite the precautions enumerated, when the catheter was removed on the 11th day after operation there was a small fistula in the mid-portion of the repair. The urethral catheter was replaced for two weeks and the fistula progressively decreased in size. Reexamination early in April, 1948, six weeks after operation, showed almost complete healing and sterile urine, with no dysuria.



Figure 2.—Ureteral catheter in diverticulum, opaque medium injected for outline. Normal cystogram above. A.P. view.

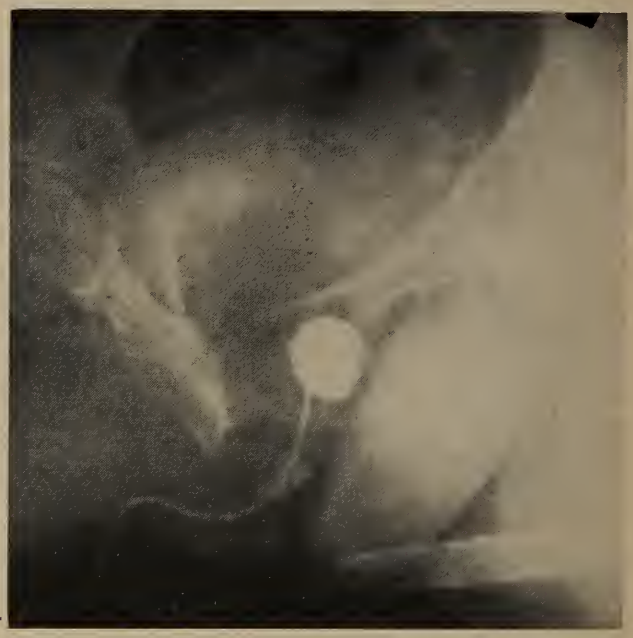


Figure 3.—Same as Figure 2 but negative shadows of calculi may be noted within diverticulum. Oblique view.

CONCLUSIONS

The origin of diverticulum of the female urethra is usually infection of urethral glands followed by periurethral abscess and sac formation.

Calculus formation in diverticulum of the female urethra is relatively rare and usually occurs from infected urine with stagnation and precipitation of urinary salts.

Diagnosis is aided by roentgen studies including the subpubic area.

Treatment is radical excision of the sac and contained calculi with repair of structures, using fine sutures over a urethral retention catheter.

Diverticulum of the female urethra with or without calculi should be considered in the presence of any chronic or recurrent urinary infection.

A case has been reported which presents most of the typical findings of this condition.

416 North Bedford Drive.

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Discussion by HENRY A. R. KREUTZMANN, M.D., *Los Angeles*

As Dr. Zide has shown, there is at present considerable controversy in the etiology of urethral diverticulae. It is too often impossible to determine from the history or from pathological examination of the excised tissue whether the sac is acquired or congenital. Most urologists are of the opinion that there is no certain method of establishing the origin of a sac.

Contrary to Johnson's belief, it is the consensus today that most diverticulae and pseudo-diverticulae are acquired. It must be remembered that not all cases present symptoms and the diverticulae then can be found only after a thorough examination. Where the sac is small and walled off, no manifestation of such a condition may be apparent. We recall one case where a diverticulum became perceptible only during the latter months of pregnancy. It grew so large as to cause the obstetrician some concern. However, after delivery it became much smaller and the patient refused to undergo operation as she had no urinary distress.

In the past few years, cases have been reported in increasing numbers, indicating that they too frequently have been overlooked in the past. Where a diverticulum is suspected, stripping the urethra and noting an excess of foul-smelling or watery pus at the meatus may establish the diagnosis.

Dr. Zide is perfectly correct in stating that routine cystourethroscopy should be performed in every case. For examining the female urethra, we have found that the best field of view has been obtained with the panendoscope.

His excellent report reemphasizes the need to examine the female urethra thoroughly in order not to overlook any pathological condition that may be present.

California Cancer Commission Studies*
Chapters XXIV and XXV

Cancer of the Bladder

A. J. Scholl, M.D., *Los Angeles*

Ash, after recording 3,200 cases of epithelial tumors of the bladder in the Tumor Registry of the American Urological Association, constructed the following average case from the statistics of the Registry: The patient is a white man aged 60. The chief complaints are hematuria and dysuria. Cystoscopic examination reveals a single papillary tumor located on the posterior surface of the base of the bladder. Pathologic study reveals papillary carcinoma, grade I or II. The prognosis is repeated recurrence in spite of treatment; the patient has about one chance in three of living five years and about one chance in 25 of complete recovery.

Most of the 3,200 patients represented by these case histories have been operated upon by men skilled in diagnostic and surgical urology, men capable of carrying out the type of treatment best suited for each individual case. Under these circumstances and with these figures before us, tumor of the bladder appears as an extremely lethal disease. In large part this depressing mortality is not due to the lack of response to treatment, or the incurability of bladder tumors, but to the excessively long period of time in which the tumors were allowed to progress unmolested. In a report of over 200 cases published in 1946, it was stated that an average of 12 months elapsed from the time the patient had the first symptoms "pointing the accusing finger at his bladder" until he presented himself to the urologist for diagnosis and treatment. In a published report of 135 cases of bladder tumor seen at the Los Angeles County General Hospital, 36 were so far advanced that no satisfactory treatment could be employed and in eight cases merely palliative cystotomy was undertaken. In all of these 44 cases, almost one-third of the total entry, the patients died in the hospital.

Another interesting commentary on the usual delay in the diagnosis and treatment of these tumors is that only 112 of 658 Registry patients (18.5 per cent) came under observation when the tumor was less than 2 cm. in diameter. This delay in receiving treatment in some cases is due to the lack of understanding of the portent of the symptoms on the part of the patient. One woman had blood in the urine almost continuously for ten years from the age of 40 to 50 years. She considered this to be an unusual type of menopause and did not seek treatment until sacral metastases caused severe pain.

In a fairly large number of cases delay is due to inaction, reassurance or symptomatic treatment on the part of the physician. It is not uncommon, by any means, to see patients who received advice and medical treatment for hematuria and bladder symptoms for years before cystoscopy finally is done. In some cases a urologic examination is suggested by the physician but not insisted upon: *it should be the duty and obligation of the physician who first sees these patients to make certain that the cause of hematuria or other symptoms is immediately determined.* Early observation would also aid the examining urologist, as the best time to determine the source of the bleeding is during the first attack, while the patient is still bleeding. Delay permits the growth to increase in size and to spread to layers in the bladder wall from which metastasis readily occurs.

CLINICAL DATA

Age and sex. The age of the patient is important; young adults stand the shock of operation well, but they often have extensive growths of a high degree of malignancy. In infants and in persons more than 60 years of age, the operative mortality is very high. In the Bladder Tumor Registry, which represents the age incidence in this country, the peak is reached between the ages of 60 and 64 years. Of 921 epithelial tumors, 160 (17.4 per cent) occurred at this age period. Of the 921 registered, 61.8 per cent occurred between the ages of 50 and 69 years.

The sex incidence of bladder tumors has been well established and seldom varies in published reports. Of 902 epithelial tumors of the bladder in the Carcinoma Registry, 684 (74.3 per cent) were found in the male, 213 (23.7 per cent) in the female; in five cases the sex was not stated. It has been found that among patients under 50 years the tumor in both sexes was of high degree of malignancy in 50 per cent of the cases, whereas among the patients after the age of 50, carcinoma of low grade predominated. There seemed to be no relation between sex and grade of malignancy.

Size of tumor. The size of the tumor when first seen is related to the result at the end of five years. In one hundred and twelve of 658 Registry tumors which were less than 2 cm. in diameter when first seen, the largest percentage of five-year "cures" was obtained, namely, 34 cases (30.3 per cent). When the tumor varied from 2 to 5 cm. in diameter, 82 of 309 patients, or 26.5 per cent, survived five years. However, when the tumor was larger than 5 cm., in only 35 of 222 cases (15.8 per cent) was the growth under control for five years.

*Organized by the Editorial Committee of the California Cancer Commission.



Figure 1.—Small pedunculated papilloma, base of the bladder.

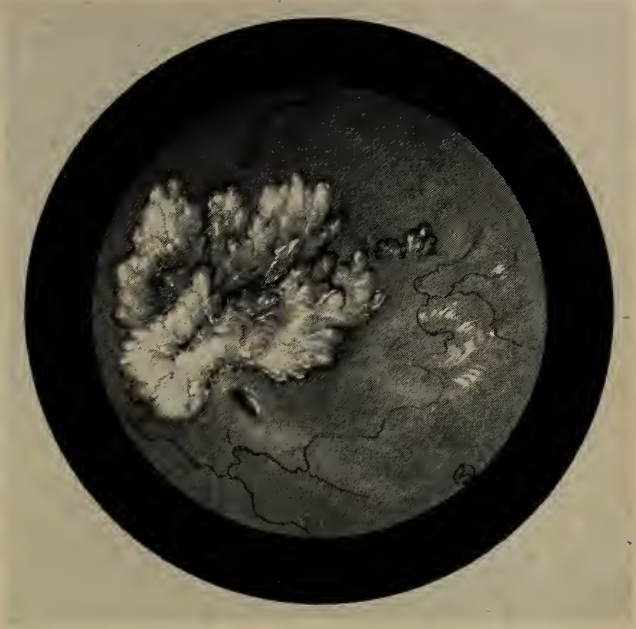


Figure 2.—Papillary carcinoma, grade II malignancy.

Location of tumor. About one-third of all tumors occur in the area of the trigone and about an equal number on the lateral walls. Ten per cent occur at the neck of the bladder and about as many on the posterior wall. A small number occur in the vault and on the anterior wall. In about 50 per cent of cases more than one area is involved.

PATHOLOGY

Practically all tumors of the bladder are epithelial in origin and may be divided into three groups; papillomas, papillary carcinomas and solid infiltrating carcinomas.

1. *Papillomas.* Simple papillomas consist of a short stalk projecting from the bladder mucosa, composed of a free, central blood supply covered with connective tissue and several layers of epithelium of adult bladder type. They vary from several mm. to 2 cm. in size (Fig. 1). *It is advisable to consider these growth not as benign lesions but as low grade epitheliomas.* Regardless of the gross or microscopic appearance many of these tumors are clinically malignant; they metastasize and recur frequently and even though early microscopic sections show no evidence of malignancy, the recurrences and metastatic deposits reveal definite malignant changes.

2. *Papillary carcinomas.* These tumors, called malignant papillomata by some pathologists, are limited in size only by the capacity of the bladder. They retain their pedicle and are composed of clubbed fronds with a marked irregularity of outline (Fig. 2). They are of a moderate degree of malignancy. In one group of 71 patients with papillary carcinoma of the bladder 26 (36.6 per cent) were dead after an average postoperative period of 11.5 months. Twenty (76.9 per cent) of those who died from malignant papillary carcinoma died in the first year after operation; 45 patients (63.3 per cent) were living an average of two years following operation.

3. *Solid carcinomas.* These tumors are of two types: the widespread papillary epithelioma, and the low, flat, infiltrating carcinoma (Fig. 3). The former has a rolled-out advancing border, the upper surface often being covered with short, stubby, papillomatous protrusions, or the top may have sloughed off, leaving a flat, ulcerated surface. These tumors, sometimes firm, are often soft, flabby and friable, and can easily be scraped off the surface of the bladder. The histological picture shows the relation of this tumor to the papilloma. In the infiltrating type the margins slope outward to meet the mucosa and burrow down into the wall of the bladder. These tumors are generally firm and compact, and without a tendency to split in cleavage planes. These solid carcinomas are the most malignant of the epithelial growths of the bladder. Sixty-seven (71.2 per cent) of a group of 94 patients with solid carcinoma were dead after an average postoperative period of 7.5 months. Fifty-nine (88 per cent) of these died the first year after operation. Twenty-seven living patients have lived an average of three years and three months.

There are a number of rarer tumors of the bladder, such as squamous cell carcinoma, adenocarcinoma, myxoma and sarcoma, which are of clinical as well as histologic interest. Benign ulcers may occur in association with infection (Figure 4).

Squamous-cell carcinomas. These tumors are distinct individual types of epithelial growths. Their onset is insidious, their growth is rapid, and they cause few distinctive symptoms. They probably develop from metaplastic bladder mucosa which has undergone epidermization as a result of irritation from infection or formation of stones. The tissue in most cases is firm and friable. The growths involve the wall of the bladder extensively, and are flat and frequently ulcerated; the lateral margins

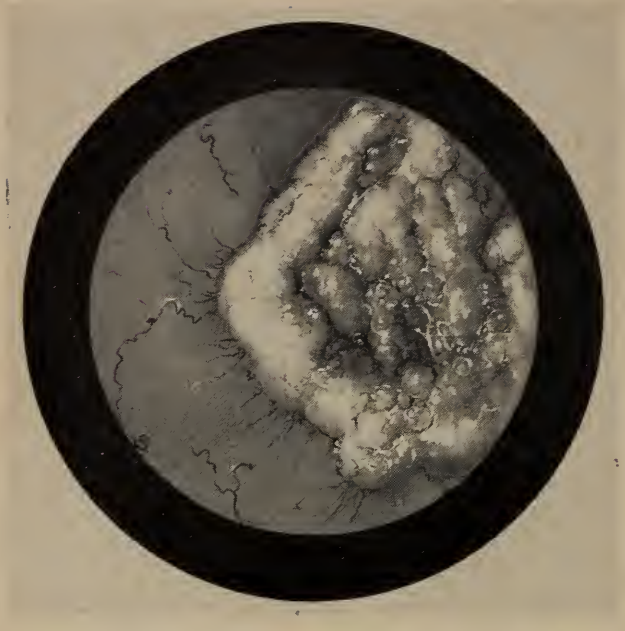


Figure 3.—Solid carcinoma in the left bladder base obstructing outlet of left ureter.



Figure 4.—Benign ulcer of bladder associated with urinary tract infection.

slope out toward the mucosa, sinking deep into the underlying tissues. Sometimes patches of leukoplakia, giving a clue to the origin of the malignancy, are found in the region of the tumor. Squamous-cell growths are most often found in early middle life and are not uncommonly preceded by evidence of long-standing cystitis. Compared with other epithelial tumors, these growths occur relatively more often in females. While metastasis is not uncommon, death in most instances is due to the obstruction and infection resulting from the local lesion. The histological examination generally shows marked cellular activity.

SYMPTOMS

Hematuria. Hematuria is the cardinal symptom of tumor of the bladder. It is the most important first signal to the patient or his doctor that a bladder tumor may be present. *It is the red flag of danger that, disregarded on first appearance, may not show a second time until the growth has progressed to a dangerous stage.*

The characteristic hematuria of tumor is spontaneous, profuse, painless and total. Tumors located near the vesical outlet may bleed slightly with onset of micturition or there may be terminal bleeding. Usually the period of bleeding is short and brisk and the interval between spells varies from days to months. This bleeding may be the sole symptom of tumor for a long time, and, as Keyes states, its very character encourages both patient and physician to pretend to themselves that the bleeding is unimportant. The tumor bleeds briefly. The patient takes a "sure" cure. The bleeding stops. It is agreed to wait to see what will happen next. A year goes by before any decision is reached —a year in which the tumor is growing, becoming larger, more difficult to control.

It is difficult to believe that of 508 cases from the carcinoma registry with initial hematuria, only half were diagnosed in the first year. Moreover, 20 per cent had to wait three years for a diagnosis and 26 cases actually were not diagnosed for seven years or more. In only one-third of these cases did the patient survive five years or more. In contrast to this surprisingly low survival in these late cases is a group of reported cases in which 142 patients with bladder tumors were cystoscoped and treated shortly after the first attack of hematuria; in all but three cases the growths were small early tumors which responded readily and favorably to treatment.

Dysuria and frequency. Painful or frequent urination is not a common accompaniment of bladder tumors, especially in the early stages of the disease. In the Registry group of cases, frequency, occurring in 15 per cent of cases at the onset of the disease, occurs in 70 per cent of cases later. This later increase is due to infection and obstruction and in some cases to extensive involvement of the bladder. In many cases there is surprisingly little bladder pain even in cases where only a small amount of bladder mucosa remains. This lack of pain is responsible for much of the procrastination in seeking treatment. Many people believe that nothing serious can occur without pain. It is not unusual to find patients who, having ignored intermittent attacks of frequency and hematuria for years, apply immediately for treatment when an extension of the growth causes pain.

DIAGNOSIS

Single or repeated attacks of spontaneous hematuria suggest the diagnosis of tumor, and the diagnosis is made by cystoscopy. Between bleedings the urine may be blood tinged or red blood cells may be found microscopically, although the absence

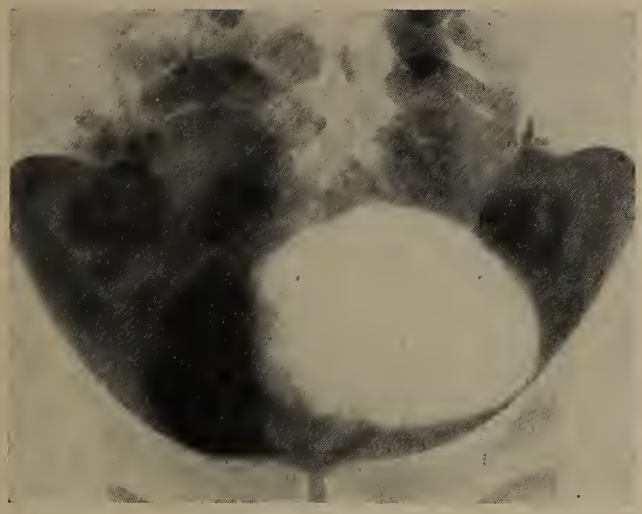


Figure 5.—Cystogram revealing comparatively small papillary tumor of right base.



Figure 6.—Papillary carcinoma of large size. Tumor was pedunculated, of low degree of malignancy, and a good result was obtained following its removal.

of blood cells does not indicate that there is no tumor. *All patients with hematuria should be cystoscoped* by one skilled in this procedure. It is essential that the examination be painless for the examiner's sake as well as that of the patient. If there is pain with cystoscopy, not only does the patient suffer but it is also impossible for the cystoscopist to make a thorough examination. Intravenous pentothal or caudal anesthesia usually gives sufficient anesthesia for an accurate, unhurried examination. The number, size, and locations of the tumors should be noted, the base or pedicle observed and a specimen of the tumor removed for histologic examination. Cystograms are helpful in estimating the extent of vesical involvement as shown by filling defects. It may show a much more extensive involvement than would be noted by cystoscopic examination and it is also helpful in the presence of a massive pedunculated tumor when an accurate cystoscopic



Figure 7.—Solid carcinoma covering upper third of bladder surface.

estimate cannot be made of the actual involvement of the vesical wall (Figures 5, 6, 7, 8, 9).

It is not always possible or desirable to catheterize the ureters, but some knowledge of the upper urinary tract should be obtained. This data can be obtained with an intravenous urogram which is of great help in determining the patency of the ureters and also gives a fairly accurate indication of the function of each kidney.

Hematuria in men of an age at which prostatic obstruction occurs is very commonly thought to be prostatic in origin, and on this account examination is at times delayed. One patient, an intelligent physician, aged 56, had repeated attacks of hematuria over a period of two years. He had been told the bleeding was probably prostatic, so cystoscopy was delayed. When finally it was done, there were one large papillary tumor on the lateral wall, numerous small tumors in the base and the entire prostatic urethra was filled with small papillomata.

All bladder tumors should be considered as potentially malignant. The size, location, number of tumors and the degree of penetration of the growth can be determined at the first examination. At this time a biopsy specimen should be taken.

It is not always possible by cystoscopy to determine the size of the base of the tumor or the degree of penetration into the bladder wall, for, in some cases, a tumor which appears to cover a large area of the bladder wall may be found on surgical exploration to have a small, compact pedicle. Bimanual pelvic examination should always be done, as in this way an estimate can be made of the extent of tumor infiltration especially about the bladder neck, the trigone, and the fundus.

Satisfactory equipment should be available to coagulate or treat the tumor if it is of a size to be

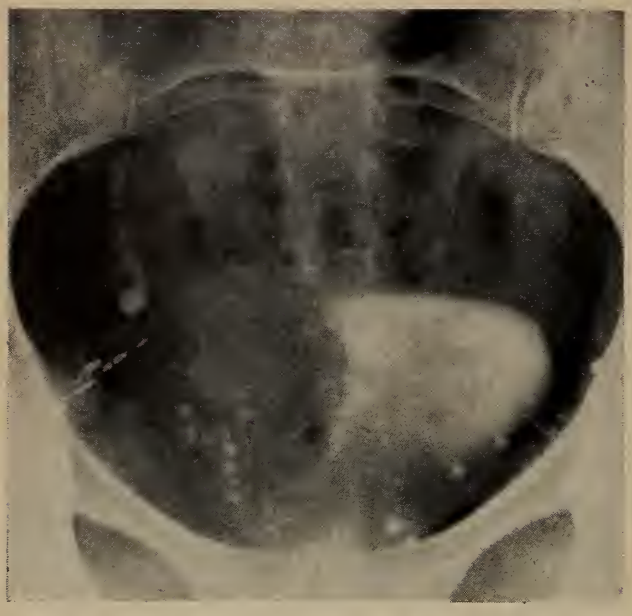


Figure 8.—Solid carcinoma of right side of bladder.

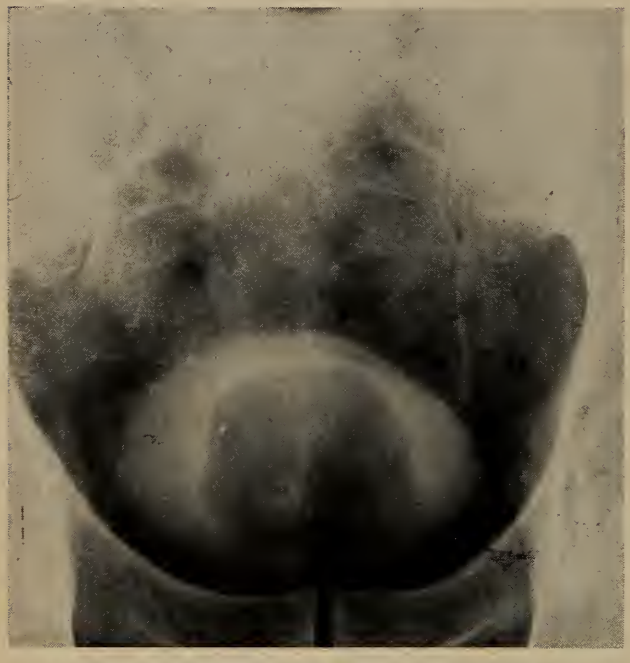


Figure 9.—Filling defect caused by hypertrophied prostate.

controlled by simple measures; if not, the required method of treatment should be decided on at this time. This is a procedure requiring considerable skill for proper performance.

TREATMENT

Collected groups of statistics indicate that treatment for tumors of moderate or large size is followed by a high mortality. Usually the patients requiring surgical operations are seen late in the course of the disease. The great majority of tumors requiring operation started as small papillomata of a low degree of malignancy which would have been readily amenable to treatment by simple transurethral procedures. The number of cases of papillomata, potentially malignant, but successfully treated by a skillful urologist as a routine office procedure is far greater than the number requiring extensive surgical operations. Certainly many cases are treated in the early stages with excellent results. The important thing is to find more of these cases, or all of them, while they are amenable to the simpler methods of treatment; when this occurs extensive surgical procedures will rarely be necessary.

The method of treating bladder tumors has changed rapidly in the last two decades and at present it varies considerably in different clinics. Exponents of certain methods of treatment such as x-ray and radium therapy and cystectomy have reported improved results in the treatment of their cases and thus influenced the general trend of treatment for a period of time. There is no single procedure that is suitable for all cases. *The best results have been obtained by operators with experience and judgment who are able to select the best treatment or combination of procedures for each individual case.*

The following methods of treatment of bladder tumors are most commonly employed at the present time.

1. *Transurethral procedures.* Transurethral procedures such as fulguration implantation of radium emanation seeds and removal of the tumor with the resectoscope should be done only in those areas that are readily accessible through the cystoscope. Papillomas up to 2 cm. in size can usually be controlled by simple fulguration. Larger tumors are generally considered malignant; nevertheless many, if they are not too large, respond to fulguration. If the tumor does not respond to three or four fulgurations, some other method of treatment is desirable.

For tumors too large to respond to fulguration transurethral resection when used by operators skilled in the use of the resectoscope gives good results especially with tumors of a low grade of malignancy. The removal of a solid tumor from a thin walled bladder with proper coagulation of the base is a delicate and risky procedure that calls for a high degree of technical skill. Recently many cases have been reported treated by this method with good results and low mortality. The tumor is resected sufficiently deep to expose the muscular layer of the bladder wall and this area then coagulated. Tumors weighing as much as 100 gm. have been removed in this manner. Following resection of tumors with a large base or those which have infiltrated the bladder wall, radon seeds may be implanted in the coagulated area as a further aid toward preventing recurrence. It is only in exceptional cases that the use of the prostatic resectoscope by the average operator is indicated. Many urologists advise against its use, favoring open methods of treatment.

2. *Suprapubic treatment.* The type of open surgical treatment employed depends on the extent and location of the growth. About 40 per cent of tumors occur on the lateral walls and in the vault, areas suitable for the removal of a segment of the entire vesical wall through a suprapubic opening. The

best results are obtained with this method of treatment, often called segmental resection, and it should be carried out whenever possible. The tumor and the entire thickness of the bladder wall should be resected with a cutting current which aids in the control of hemorrhage and avoids the spread of tumor cells in the operative field. A margin of normal bladder wall 1 cm. or more in width around the periphery of the tumor should be included in the resection. If the growth is comparatively small, or of a low degree of malignancy, or if it is an area unsuitable for resection, it may be excised with a portion of the bladder wall. The base is then thoroughly coagulated with a diathermy electrode and radon seeds planted if further treatment seems necessary.

Electrocoagulation or diathermy is the method of choice in destroying the flat, fairly extensive papillary growth of a low degree of malignancy. Occasionally growths which are apparently so extensive as to be inoperable respond surprisingly to thorough coagulation. On this account coagulation should be carried out, if possible, in patients with tumors that are seemingly inoperable; in a number there will be regression of the tumor.

There is a small group of cases in which the tumor is still confined to the bladder but is so located or so extensive as to preclude any possibility of cure by the usual methods of treatment. Cystectomy has been done in a number of these cases and reports of results have been increasingly more favorable. The mortality is high and the survival rate low, although in a group of recently reported cases satisfactory results have been obtained. Cystectomy demands that the urinary stream be diverted, which is usually carried out as a preliminary procedure. The bladder is then resected at a second operation. In some cases both procedures have been carried out at the same operation.

3. *Irradiation therapy.* High voltage x-ray therapy should be reserved for use in inoperable cases, for palliation and the arrest of hemorrhage. It is best suited to cases with a high degree of malignancy, as radiosensitivity tends to increase in proportion to malignancy. In occasional isolated instances x-ray therapy produces startling regression of the tumor. In those cases where, for various reasons, other more dependable methods cannot be employed, it may be of benefit.

There is little evidence to show that malignant tumors of the bladder can be cured by high voltage irradiation. Most urologists believe that it should be used only for patients who have advanced tumors, or for old and debilitated patients. In any case in which operation is suitable, it should be done.

4. *Implantation of radon.* Radon seeds have a definite place in the treatment of tumors of a high grade of malignancy. These seeds may be used in association with irradiation but they are most frequently employed following electrocoagulation. In tumors where seeds have been planted preoperatively through the cystoscope the proliferative power of the tumor cells, as observed postoperatively, is markedly reduced and in some cases completely destroyed. In other areas, nests of apparently intact malignant cells may be found. What benefit might be obtained by preoperative treatment is nullified by the increased technical difficulty of later surgical removal. The edema, swelling and friability of the irradiated tissue make it difficult and at times almost impossible to resect and close the bladder wall. On this account preoperative radium treatment is now rarely used.

SUMMARY

Tumors of the bladder, when treated during the early period of symptoms, respond readily to treatment and results can be obtained which are comparable to those obtained following treatment of tumors occurring in other parts of the body.

Intermittent hematuria is the most frequent and outstanding symptom of bladder tumor. Its prompt and complete, temporary disappearance, together with the lack of pain and discomfort, gives the patient and often the physician a false sense of reassurance, inviting procrastination in examination and treatment. Unfortunately, bleeding may not recur until a regrettably long period of time has elapsed.

Hematuria is always serious; it should never be ignored without definitely determining its origin. This necessitates a cystoscopic examination. If this is done as a routine measure, it will be possible to reduce substantially the distressingly high mortality from tumor of the bladder.

Given an early case, the chance of cure for the patient with a bladder tumor is dependent in large part upon the skill, knowledge, and experience of the cystoscopist.

"Cysts and Tumors of the Jaws," by Eugene W. Demaree, M.D., Chapter XIIA of the California Cancer Commission Studies will appear in this section of the January number of California Medicine.

Correction

The name of one of the authors of Chapter XXII of the California Cancer Commission Studies, which appeared in the September issue of California Medicine, was misspelled. The chapter, titled Carcinoma of the Liver, Gallbladder, Extrahepatic Ducts, and Pancreas, was written by William F. Roe, M.D., of Van Nuys, and E. Eric Larson, M.D., of Los Angeles. Dr. Roe's name was misspelled "Rowe."

Cancer of the Prostate

Roger W. Barnes, M.D., *Los Angeles*

EVERY man who presents himself for physical examination should receive the benefit of digital palpation of the prostate through the anterior rectal wall. Routine investigation by this method familiarizes the examiner with the consistency, size, contour and sensitiveness of the normal gland, thus enabling him more readily to distinguish pathological changes, the most important of which is early malignancy.

Cancer of the prostate is found in 15 to 20 per cent of patients who have urinary obstruction due to prostatic enlargement. Some investigators have reported that 20 per cent of all men over 50 years of age have cancer tissue in the prostate gland but the majority of these die of other diseases before prostatic difficulties develop.

The pathological process usually originates in the dorsal portion of the prostate, near the capsule at its apex (the so-called posterior lobe), and may invade the entire gland from this point. It may, however, begin at any place in the gland. Sometimes islands of malignant tissue are found surrounded by benign hyperplasia, or the dorsal portion near the capsule may be malignant and the remainder of the gland benign. Cancer extends beyond the prostatic capsule early in the disease. Therefore, by the time a definite diagnosis can be made the lesion in most cases has extended too far for cure to be effected by radical prostatectomy. Later in the course of the disease, the neoplasm extends upward under the trigone, involving the seminal vesicles and encroaching upon the bladder neck, causing urinary obstruction.

The degree of malignancy of the neoplastic tissue determines the gross consistency of the gland and influences the prognosis. Most prostatic carcinomas are grade II (based on a four-grade classification), and are very hard and fixed. A few are grade IV, and these so resemble benign hyperplasia on rectal palpation that often the correct diagnosis of malignancy is not made preoperatively. When the process is highly malignant there is a shorter life expectancy.

Metastases to bone are of frequent occurrence late in the disease and are most commonly found in the pelvis. Usually they are osteogenic (increased calcium deposit); however, if the malignancy is high grade the bone lesion is osteolytic (decreased calcium deposit).

SYMPTOMS

The symptoms produced by carcinoma of the prostate are seldom manifested in the early stages of the disease. They are of two kinds; (1) obstructive, due to growth of the tumor into the prostatic urethra and bladder neck; and (2) pain, due to local extension or metastasis to bone.

Obstructive symptoms are usually first noticed by the patient, although occasionally a far advanced malignancy may be found without bladder disturbance. Urinary frequency, burning, slowness of the urinary stream, and irritation at the bladder neck are the presenting symptoms when the vesical outlet is encroached upon by the prostatic tumor. These may occur relatively early in the course of the disease if the cancer is associated with hyperplasia of the gland; in such cases symptoms are due chiefly to the benign lesion. When the obstruction is caused solely by the cancer, it occurs in the more advanced stage of the disease. Urinary tract infection, determined by the finding of pus and mixed microorganisms in the urine, usually develops when obstruction and residual urine have existed for a time. If this condition is allowed to persist for several years, dilatation of the upper urinary tract and impairment of renal function result.

Symptoms due to extension of the malignancy do not occur until the disease is advanced. Perineal or rectal pains or consciousness of this area may be the first symptoms. Low backache, pain in the groins, external genitalia, perineum and thighs, and later edema of the lower extremities are characteristic and may be very severe and constant. General malaise, weakness, loss of weight, and enlarged inguinal lymph nodes occur in the later stages of the disease, but are not usually present until the malignancy is widespread. Occasionally bone metastases occur beyond the pelvis and spine; when this takes place pain appears in the areas involved. Blood in the urine is never an early symptom or finding. It does not occur until the neoplasm has extended through the bladder or prostatic urethral mucosa, and even then it is not a constant finding. In fact, this symptom is much more common in benign hypertrophy than in carcinoma of the prostate.

DIAGNOSIS

If carcinoma of the prostate is to be cured by radical surgical operation, it is necessary that complete extirpation be accomplished before the neoplasm has extended through the perineural sheaths beyond the capsule. Because extension occurs early, the correct diagnosis must be made before the disease is advanced in order that it may be eradicated by operative removal. A presumptive diagnosis of carcinoma of the prostate in most cases can be made by digital palpation of the gland through the anterior rectal wall. *Inasmuch as the neoplasm most commonly originates in the dorsal portion of the prostate near the capsule, a hard, fixed nodule felt in this area is suggestive of malignancy.* The great difficulty in arriving at a diagnosis in early cases is that on palpation a localized area of inflammatory induration is often indistinguishable from a malignant nodule. It is impossible to make a positive early diagnosis by rectal palpation alone; careful histopathological study of the suspected area is the only means of establishing the diagnosis at this stage.

In order to obtain a satisfactory specimen for histopathological examination, the capsule of the prostate must be exposed through a perineal incision, the nodule identified and removed and a rapid frozen section made. If the tissue is found to be neoplastic, a radical perineal prostatectomy is done; if it is inflammatory the wound is closed without removal of the prostate unless there is obstruction due to benign hypertrophy. Opinion among urologists differs as to the advisability of this procedure. Some believe that every patient in whom a suspicious nodule is palpated should have immediate perineal exploration. Others maintain that this procedure is too radical because in a large proportion of cases microscopic examination discloses inflammatory induration rather than malignancy, and also that total perineal prostatectomy does not cure the disease in enough patients to be worth the risk entailed. It is wise for the physician to share the responsibility of making a decision in these cases by explaining the facts to the patient and by obtaining an opinion from a competent urologist.

Aspiration biopsy by needling the suspected area through the perineum and attempting to withdraw tissue cells for microscopic study is unreliable and is almost never indicated. Procurement of a specimen by endoscopic prostatic resection is not indicated unless bladder neck obstruction is present and the operation is directed primarily toward relief of the obstruction.

Carcinoma of the prostate is easily diagnosed in most cases in which the disease has progressed beyond the early stage. The characteristic stony hard and fixed gland as palpated by rectum is almost diagnostic; when the gland is irregular, nodular and enlarged the evidence is still more conclusive.

There are two conditions which must be differentiated from carcinoma: (1) Subacute prostatitis, which may present the same palpable characteristics as malignancy, especially when there is inflammatory induration of the periprostatic tissues. The onset of symptoms, however, is usually more acute, there is greater frequency and burning on urination, and a low grade fever is nearly always encountered. (2) Prostatic calculi, which are stony hard to rectal palpation, whereas the prostate as a whole is more movable and some elasticity is noticeable over the hard mass of calculi.

The prostate may contain malignant tissue yet not be hard and fixed on rectal palpation (1) when malignancy is high grade, as explained later in this chapter, in the section on "Pathology," and (2) when there is an island of neoplastic tissue surrounded by benign hyperplasia. Both these situations are comparatively rare.

Residual urine is found when there is bladder neck invasion by the neoplasm and when associated benign prostatic hypertrophy is sufficient to obstruct urinary outflow.

Cystoscopic examination is of some value in diagnosing prostatic malignancy in advanced cases but does not aid in the identification of early ones. When the prostatic urethra and bladder neck are invaded by the neoplastic process, rigidity of the vesical orifice is present, and nodules with prominent blood vessels in the mucosa which encroach into the urethral lumen, bladder neck and trigone (if the latter has been invaded) can be seen through the cystoscope.

Bone metastases are nearly always easily diagnosed by roentgenograms. However, metastatic deposits in bones or tissues may produce pain without being evident on x-ray films. Mottled areas of increased ossification (osteogenic) are seen in the roentgenogram of the pelvic bones. Sometimes the changes extend to the spine and ribs, and occasionally all the bones of the body are involved. If the prostatic malignancy is high grade, these bone changes may consist of areas of rarefaction (osteolytic). A comparatively new method of testing for metastases to the bones from carcinoma of the prostate is that of determining the acid-phosphatase content of the blood. When this is more than 4 mg. per 100 cc. it suggests such extension; if it is above 10 mg. it is practically diagnostic. Carcinoma of the prostate without bone metastases almost never produces an elevation in serum acid phosphatase. Alkaline phosphatase may be elevated with soft-tissue extension.

TREATMENT

Since the advent of endocrine therapy for carcinoma of the prostate, the outlook for patients who suffer from this disease is much brighter than formerly. There are five different courses of action which urologists now follow:

a. Immediate castration plus large doses of estrogens.

b. Estrogens alone as long as symptoms are controlled and there is no evidence of extension of the disease. Castration is thus reserved until the beneficial effect of the estrogen is lost.

c. Immediate castration, with administration of estrogen withheld until the disease extends.

d. Castration after extension of growth or metastasis is manifested, with estrogen prescribed later to neutralize androgens produced by adrenals.

e. Reduction of androgen production by exposure of the testicles to x-ray. This is used by only a few urologists and is probably not as effective as the administration of estrogens or surgical castration.

The most common and convenient method of administering estrogens is to give stilbestrol by mouth. The recommended initial dose is from 5 to 10 mg. per day, usually 2 mg. three times daily. If this medication causes nausea or gastric distress, enteric coated tablets can be given. These may not be effective if the coating does not dissolve and the tablets pass through the bowel without absorption. When excessive soreness of the nipples develops the dose is reduced to tolerance. It is continued indefinitely in maintenance doses of from 2 mg. a day to 2 mg. a week, usually about 1 mg. daily. When the patient cannot tolerate medication by

mouth, some other estrogen, such as estradiol dipropionate, 10 mg. daily as an initial dose, is given hypodermically.

When orchiectomy is performed, it is advisable to leave the epididymis on each side for esthetic reasons; the patient does not feel so emasculated if part of the scrotal contents is allowed to remain, even a small part. Sometimes the testicular tissue is removed and the entire tunica of the testes as well as the epididymes is left. Other urologists prefer the simplest and quickest procedure. From a medicolegal standpoint, it is not wise to perform castration unless the diagnosis of malignancy has been confirmed by histopathological study or by x-ray findings of bone metastases and elevated serum acid phosphatase.

Ten to 20 per cent of patients do not respond to endocrine therapy. However, in those who are susceptible to this treatment, the immediate results are almost miraculous. Within a week following the beginning of treatment the patient's pain has subsided and his appetite has returned; within two weeks he begins to gain weight and strength, and soon thereafter the enlargement and hardness in the prostate as palpated by rectum begin to melt away and urinary obstructive symptoms abate. If bone metastases have been demonstrated by x-ray these may disappear in a few months and in many cases every sign and symptom of the disease disappears. The unfortunate feature is that these changes represent only a temporary regression of the disease, not a cure. In some patients symptoms begin to reappear within a year; in others apparent absence of the disease may last eight or ten years.

For the group of patients who do not respond to estrogenic therapy, and for those who have recurrence of symptoms regardless of continued treatment, deep x-ray therapy is sometimes useful to relieve pain and to retard the malignant process. The administration of analgesics and other palliative measures are used to relieve pain. Permanent suprapubic cystostomy, indwelling urethral catheter, or frequent catheterization is necessary if urinary obstruction persists.

Radical perineal prostatectomy for removal of early prostatic malignancy has been discussed in the paragraph on diagnosis. In late cases the surgical treatment of this disease is concerned chiefly with the relief of vesical neck obstruction. Before transurethral prostatic resection was a common procedure, the most usual method of relieving obstructive symptoms was to perform suprapubic cystostomy for permanent bladder drainage. This is still the method of choice in patients in whom obstruction recurs within a few months after relief by transurethral resection and in those on whom this operation cannot be done because of urethral stricture or other reason.

Many patients who present urinary obstruction due to prostatic carcinoma will be relieved of this symptom only after several weeks of endocrine therapy. It is, therefore, wise to continue this treatment for a month or more before performing an operation to relieve the urinary retention. When there is a definite associated benign hypertrophy, obstructive symptoms will nearly always persist until relieved by operation. The transurethral approach is the method of choice because carcinoma of the prostate is very difficult to enucleate either suprapubically or perineally and a cure by any type of surgical intervention is rare except in very early cases. When there are islands of malignant tissue surrounded by benign hypertrophy, transurethral resection, if carried out completely and thoroughly, will cure as effectively as enucleation; however, the latter procedure is preferable to incomplete resection. Recurrence of vesical neck obstruction is common and when this occurs repeat transurethral resection of the bladder neck is necessary. Some authorities believe that 500 to 1,000 milligram hours of radium applied locally to the prostate will retard or prevent local growth. In some cases keeping the bladder neck dilated with sounds or a Kollmann dilator at frequent intervals may obviate the necessity for repeating the endoscopic operation.

Prostatic massage is not indicated in carcinoma of the prostate, and in fact may do considerable harm by disseminating neoplastic cells. It should be avoided whenever there is a probability of this disease.

PROGNOSIS

Carcinoma of the prostate is a slow-growing malignancy in most cases and the patient may live for as long as 15 or 20 years without treatment. The grade of malignancy has a definite bearing on the prognosis. The average length of life of the patient with a grade II tumor, which is the type most commonly found, is about four or five years when treatment consists of relief of urinary obstruction alone. The man who has a grade III or IV neoplasm has a life expectancy of only one to two years after onset of symptoms. Endocrine therapy has improved this prognosis considerably, but no definite statistics are yet available. It is probable that from two to five years will be added to the life expectancy of patients who respond to this treatment.

SUMMARY

1. Digital examination of the prostate through the anterior rectal wall should be included in the examination of every male patient. The presence of one or more small hard nodules is suggestive of early malignancy and a hard fixed gland is characteristic of further advanced carcinoma.

2. Symptoms may be due to obstruction to urinary outflow or to extension or metastases causing pain.

3. The administration of estrogens or the elimination of androgens by castration, or both, results in a remission of from one to six years in 80 to 90 per cent of cases. Transurethral prostatic resection is performed to relieve urinary obstruction, and radical perineal prostatectomy may be indicated in early cases. Prostatic massage is harmful.

California MEDICINE

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EDITORIALS

The Heat's On

President Truman proved on November second that a one-man campaign, carried out in the face of apparently insuperable odds and against the glum predictions of his own followers, can be made to succeed. The nation has been stunned by the measure of success he achieved; it has admired his fighting methods even though it has had some cause to question his promises of all things to all people.

Among the promises was one to extend the provisions of the Social Security Act, an extension which has been painted and framed by his advisors and appointees in several departments of the Government. It includes, among other things, the extension of social security laws to employees not now covered by the law, the inclusion in the program of self-employed individuals (you, too, doctor), the increase of taxes against employer and employee and, certainly not least, the enactment of a national system of compulsory health insurance.

California doctors have long studied and opposed the establishment of a compulsory health insurance plan, either national or state. Now they are faced with a Democrat president and a Republican governor, both announced proponents of such a plan. If the doctors are to continue opposing a politically-operated system of medical practice, they must aim their weapons at both Washington and Sacramento.

There is no doubt that medicine has a fight on its hands. The chips are down and from now on it's a case of winner take all. Fortunately, the doctors have always won this fight and have as an advantage a string of victories and the accumulated knowledge of how they have been won. They know that other groups and organizations must be alerted to their own fate if the process of socialization is started against the medical profession. They know that the public must be advised of what is in store for Mr. and Mrs. John Q. when the heavy hand of bureaucracy takes over for bedside manners. They know that the public, once advised, will rise up in its own right and deny the right of politicians to take over for free choice of a physician who will render scientific care. They know that legislators must be particularly well advised on the implications behind this sort of vote-making machinery. Experience has taught the doctors these and many other things about socialized medicine, just as experience has taught them the bulk of what they know on the scientific side of medicine. There is room for improvement of techniques, certainly, but the old and time-tried measures will certainly form the basis for the development and application of the tactics needed now.

Some physicians have taken on a defeatist attitude since the election returns were counted. Some seem to think that, faced by both a national and a state threat, private medical practice is doomed. Some have advanced the theory that medicine had better go along with the tide and try to divert it into useful channels. Some are saying they are glad to be in their later years and on the road to retirement before the oncoming wave engulfs their sons and students.

To such as those mentioned above, perhaps Mr. Truman has served up a good example. Perhaps he has, by his own actions, proved that a good fight can always be made when you believe you have the right on your side and maintain confidence in the public. Perhaps his vigorous campaign against heavy odds has lighted the path along which medicine, as a supposed underdog, can travel to victory.

The heat's on. Let's roll up our sleeves and go to work.

Hats Off

Medical practice on the distaff side has come a long way from its former position of being tolerated if not just plain ignored by the male members of the profession. Where once the woman physician was a rarity, today we are accustomed to seeing more and more practitioners in skirts, many of them definitely in fields such as industrial medicine where doctors in trousers are usually exclusively in attendance. The gentler aspects of laboratory work and obstetrics can no longer lay sole claim to the services of our female confreres.

The ladies have advanced in another direction, too. They have entered wholeheartedly into the economic and political sides of medical practice and have proved their right to be heard and respected in these fields. Their counsel has been invaluable on many occasions.

All of which brings us to a salute to Dr. Leslie S. Kent of Eugene, Oregon, first woman physician to be honored by her fellows by election to the presidency of a state medical association. Doctor Kent has labored long in an active medical practice and in organization affairs. She took a leading part in medical dealings with the warborn EMIC program and has become well and favorably known in many medical organizations outside her own state. Her election to high office in Oregon bears out the confidence which her many friends have in her and the respect in which she is held.

Congratulations to Doctor Kent and to the Oregon State Medical Society which elected her president. Hats off to the ladies and, particularly, to our good friend Leslie Kent.

Woman Also Works

Periodically the California State Division of Industrial Welfare finds it necessary to call attention to the laws regarding the employment of women in industrial, general, business or professional offices. That time has come again and the state agency has come up with a gentle reminder that women and minors are, in the eyes of the law, a little different from men employees.

For instance, a woman employee may not be scheduled to work more than eight hours in any one day. In case of emergency she may work more than eight hours but the overtime must be paid for at one and one-half times the regular wage rate. She must be paid a minimum wage of 65 cents an hour (if you can find anyone at that rate) and must be given a regular rest period, say ten minutes, morning and afternoon. She must be allowed a meal period of not less than 30 minutes not later than five hours after she reports for work. Her starting and leaving time must be recorded, along with the number of hours worked and total wages received in each payroll period.

Some of these requirements will appear elementary to many physicians but in those rare instances where they are not lived up to, the employing doctor may run afoul of the law. To be safe, instead of sorry, write the Division of Industrial Welfare at 404 State Building, Los Angeles 4, or 865 Mission St., San Francisco 3, for a copy of Order No. 4R, which tells all about it.

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NOTICES AND REPORTS

Council Meeting Minutes

Tentative Draft: Minutes of the 356th Meeting of the California Medical Association, Los Angeles, October 30-31, 1948.

The meeting was called to order by Chairman E. L. Bruck in Conference Room 5 of the Biltmore Hotel, Los Angeles, at 9:30 a.m., Saturday, October 30, 1948.

Roll Call:

Present were President Askey, President-Elect Kneeshaw, Council Chairman Bruck, Speaker Alesen, Vice-Speaker Charnock, Councilors Crane, Henderson, Anderson, Ray, Lum, Pollock, Green, Cherry, MacLean, Hoffman, Bailey and Thompson, and Editor Wilbur.

Absent: Councilor Ball. Excused: Councilor Shipman and Secretary Garland.

Present by invitation were Dr. Dwight H. Murray, chairman of Public Policy and Legislation; Executive Secretary John Hunton; Assistant Executive Secretary William P. Wheeler; Legal Counsel Howard Hassard; Mr. Ben H. Read, executive secretary of the Public Health League of California; Mr. Ed Clancy, field secretary; Mr. James J. Boyle, Washington representative of the United Public Health League; Doctors Malcolm Merrill and Edward Kupka of the California State Department of Public Health; Doctor William Gardinier and Mr. John McMahon of California Physicians' Service, and county society executive secretaries Rollen Waterson of Alameda and Stanley K. Cochems of Los Angeles.

A quorum present and acting.

1. *Minutes:*

(a) On motion duly made and seconded, minutes of the 355th meeting of the Council, held August 21-22, 1948, were approved.

(b) On motion duly made and seconded, minutes of the 211th meeting of the Executive Committee, held August 22, 1948, were approved.

(3) On motion duly made and seconded, minutes of the 212th meeting of the Executive Committee, held September 29, 1948, were approved.

Special Recognition for 50-Year Members

Seven members of the California Medical Association have been reported by the secretaries of their county societies as eligible for the special recognition which the Council voted shall be given to those who have maintained membership in the association for 50 years or more.

Just what the token of recognition is to be has not yet been decided by the Council, but wall plaques and lapel emblems have been considered.

The seven members on the present list of eligibles are:

G. W. Duffing, Sacramento County
Andrew Henderson, Sr., Sacramento County
Herbert C. Moffitt, San Francisco County
James Seymour, San Francisco County
William Stephens, San Francisco County
W. I. Terry, San Francisco County, and
G. W. Sevenman, San Mateo County.

Eligibility is established through the records of the component county societies of the C.M.A. Any member who believes himself eligible but is not one of the seven named above is requested to call the matter to the attention of the secretary of the county society of which he is a member.

2. *Membership:*

(a) A report of membership as of October 28, 1948, showing 9,180 active and associate members, was received and ordered filed.

(b) On motion duly made and seconded, one member whose 1947 dues had been received since August 22, 1948, was voted reinstatement.

(c) On motion duly made and seconded, twenty-four members whose 1948 dues had been received since August 22, 1948, were voted reinstatement.

(d) On motion duly made and seconded, rules and regulations covering the reduction of dues for members who are absent from their practices for extended periods because of illness or postgraduate study, prepared by a special Council committee, were approved.

(e) On motion duly made and seconded, a reduction of dues was granted to seven members who were recommended for such reduction by their county societies because of illness or postgraduate study. These were:

Dean S. Scofield, Los Angeles County.
Erwin P. Brauner, Orange County.
Fred E. Abbott, San Diego County.
William M. Wilson, Jr., San Diego County.
Isabella H. Perry, San Francisco County.
W. E. Jensen, Santa Cruz County.
Thomas F. Keyes, Yuba-Sutter-Colusa County.

(f) On motion duly made and seconded, thirty applicants for affiliate membership were voted such membership on nominations by their county societies.

(g) Seven members who had been reported by their county societies as having maintained membership for fifty years or more were, on motion duly made and seconded, elected to receive an emblem honoring their long term as active members. A suitable emblem was selected and it was agreed to make the presentation at each Annual Session. The members so elected were:

G. W. Duffing, Sacramento County.
Andrew Henderson, Sr., Sacramento County.
Herbert C. Moffitt, San Francisco County.
James Seymour, San Francisco County.
William Stephens, San Francisco County.
W. I. Terry, San Francisco County.
G. W. Sevenman, San Mateo County.

3. *Financial:*

(a) A report of bank balances as of October 28, 1948, was received and ordered filed.

(b) Report was made that $130,000 in current funds had been invested in U. S. Treasury bills, which mature in 90 or 91 days, and that $25,000 in funds held by the Trustees of the C.M.A. had been invested in U. S. Treasury 2½ per cent bonds, due 1972.

4. *Memorial to P. K. Gilman, M.D.:*

The Council discussed the establishment of a memorial to the late Philip Kingsnorth Gilman, M.D., former Councilor and former President of the Association. On motion duly made and seconded, it was voted to establish a $1,000 memorial fund at Stanford University School of Medicine. It was agreed that this fund should, if possible, carry Doctor Gilman's name. Dr. Dwight Wilbur was instructed to continue his efforts to determine the most effective application of the fund.

5. *California State Department of Public Health:*

Dr. Malcolm Merrill of the California State Department of Public Health displayed charts and figures on the polio situation, pointing out that the number of cases reported in 1948 was approaching the 1934 record high and would probably pass the 1934 figure. Peak of the cases came in September, which is later than usual, and the trend is now downward.

Doctor Merrill also discussed several items which will account for the bulk of the increase in budget which the Department is seeking for the 1949-1950 fiscal year. Major items in the increase will be (1) additional sanitary engineers to handle the sewage, water and other problems aggravated by a greatly increased population; (2) establishment of schools of physiotherapy for cerebropalsy cases; (3) establishment of a pattern for state aid to the counties for crippled children's cases; and (4) increased studies of Q fever, following the withdrawal of most U. S. Public Health Service personnel at the end of 1948.

Doctor Merrill reported that the State Department of Public Health's tuberculosis control program would be well served by a committee composed of representatives of the Department, of the California Medical Association and of the California Tuberculosis and Health Association. On motion duly made and seconded, it was voted to name a representative of the Association to such a committee. The Chairman appointed Dr. H. Gordon MacLean to this position.

Doctor Merrill discussed the proposed mass mini-film x-ray survey for tuberculosis. Survey teams would be sent into California by the U. S. Public Health Service in 15 to 18 months, to make films of all people above 16 years of age in the metropolitan centers. Estimates show 6,000,000 people in these four areas, and an estimated 4,000,000 films would be made; of this number, an estimated 3½ per cent would show some chest pathology and about one case of tuberculosis per 1,000 films would be expected, about 90 to 95 per cent of this number being previously unknown. Cost would run about $500 for each active case uncovered. Active cases of tuberculosis or other chest conditions would be referred to private family physicians. Approval of the State Department of Health and of the California Medical Association would be required before the U.S.P.H.S. would undertake the survey.

On motion duly made and seconded, it was voted to defer action on this request pending further study, including the determination of the attitude of medical associations in areas where similar surveys have already been made.

Doctor Bruck reported that the Chronic Disease Study advisory committee had met and that proposed portions of the report of the advisory committee had been drafted. These will go to an editing committee which will put them into final shape for presentation to the committee. Doctor Bruck read

the preliminary proposed reports covering research, state planning and administrative research, and diagnostic and therapeutic services. Suggestions were offered for amending the preliminary drafts and the amended reports approved.

Dr. Lyell C. Kinney, chairman of the Cancer Commission, appeared before the Council and read the preliminary proposed report of the section on cancer for the same report. Amendments were offered and the amended report approved.

6. *Physicians' Benevolence Committee:*

Dr. Axcel E. Anderson, chairman of the Physicians' Benevolence Committee, requested nominations for appointment of a member to the committee, to succeed Dr. Robert A. Peers, retired. On motion duly made and seconded, it was voted to extend this appointment to Dr. John W. Sherrick of Oakland.

7. *Advisory Planning Committee:*

Mr. Hunton reported that the Advisory Planning Committee had held two meetings and had taken two actions on which Council approval was requested. (1) It was decided to make transcriptions of a radio series entitled "If They Had Lived Today," produced by Mr. Stanley Cochems of Los Angeles, and make these transcriptions available to other county medical societies which wished to use them. The Council approved this action as a part of the public relations program. (2) The Committee recommended that copies of the Brookings Institution study on compulsory health insurance be purchased and sent to all public school libraries in California. Copies would cost $1.50 each and about 2,000 copies required. On motion duly made and seconded, the Council voted to approve this program and expenditure.

8. *Committee on Scientific Work:*

A resolution clarifying Council instructions to the Committee on Scientific Work regarding the number of C.M.A. guest speakers invited to Annual Sessions was presented. Five guest speakers are now authorized. Sections sometimes wish to invite outstanding speakers in their own fields, expenses of such being borne by members of the section or specialty group; in some instances such guests might be regarded as official guests of the Association itself. On motion duly made and seconded, it was voted that guest speakers beyond the authorized five each year, may be invited by specialty sections, the question of whether such guests are to be considered as guests of the Association to be decided by the Committee on Scientific Work.

9. *California Physicians' Service:*

Mr. John McMahon, assistant director of C.P.S., reported that as of October 1, 1948, membership in C.P.S. totaled 615,444 in the commercial program. September enrollment was 25,060, of which 40 per cent was new membership groups and 60 per cent additions to existing groups. Individual enrollment is being tried out in Eureka and experience to date shows that individuals will not respond to newspaper advertising or radio appeals but must be individually solicited.

Dr. William Gardinier, assistant medical director, reported that physician membership as of October 1, 1948, was 9,178. The financial report as of September 1, 1948, showed $416,000 in the unit stabilization fund reserve and showed that $5,000,000 had been paid to physicians for their services in the first five months of the present fiscal year.

There was discussion relative to C.P.S. and it was regularly moved, seconded and voted to include in the next Council meeting a joint session with the trustees of C.P.S.

10. *Blue Shield-Blue Cross Proposals:*

Mr. Hassard discussed the recent meeting in French Lick Springs, Indiana, of the Blue Shield and Blue Cross plans, at which a proposed establishment of a national enrollment agency was under consideration. The conference resulted in three decisions: (1) That a national organization be discussed but not acted upon at that meeting. (2) That Blue Shield member plans discuss the national organization proposal with their own sponsoring state or county medical association, and (3) that the proposal be referred to the A.M.A. House of Delegates by a committee appointed to make such presentation in conjunction with the A.M.A. Council on Medical Service.

The American Hospital Association has approved the proposed national organization, in which the Blue Cross Commission of the A.H.A. would participate. The Blue Cross plans voted at the recent French Lick meeting not to go ahead on plans of their own for establishment of a national program offering hospitalization and medical-surgical indemnity until the A.M.A. House of Delegates has had a chance to consider the proposed joint program; in the event the A.M.A. votes against the proposed plan, the Blue Cross plans have indicated their intention to establish their own national enrollment program but in this case have agreed to leave the way open for Blue Shield plans to participate if a later decision makes this possible.

On motion duly made and seconded, it was voted to recommend to the California Delegates to the American Medical Association that they vote against the proposed national enrollment organization plans unless the medical phases of such plans are placed directly under the control of the A.M.A.

11. *Emergency Medical Service:*

On motion duly made and seconded, it was voted to appoint a committee of five as a Committee on Emergency Medical Service, to cooperate with the Committee on National Emergency Medical Service of the American Medical Association. The Chairman, authorized to make such appointments, appointed Drs. L. A. Alesen of Los Angeles, chairman; Carleton Mathewson, San Francisco; Lewis T. Bullock, Los Angeles; Frank A. MacDonald, Sacramento; and Orris R. Myers, Eureka.

12. *Blood Banks:*

The Chairman read a progress report from Dr. John Upton, chairman of the Blood Bank Commission, and the report was received and ordered filed.

13. *California Medicine:*

Dr. Dwight L. Wilbur, editor of CALIFORNIA MEDICINE, reported that a proposed publication of annual medical reviews by a Chicago physician and his associates did not appear feasible for inclusion as a supplement to CALIFORNIA MEDICINE and that he had suggested to the authors that paid advertising might be run to promote its sale. It was regularly moved, seconded and voted that this publication should be considered as a commercial venture, eligible for advertising in the journal.

Mr. Hunton, on behalf of the advertising committee, requested clarification of the Council attitude toward the acceptance of liquor advertising. It was regularly moved, seconded and voted that alcoholic beverage advertising be not accepted pending further action by the Council.

At this point, 1:45 p.m., the Council recessed until 9:30 the following day.

14. *Reconvention:*

The Council reconvened at 9:30 a.m., Sunday, October 31, 1948, in Conference Room 5 of the Biltmore Hotel, Los Angeles. A roll call showed all those present the preceding day to be present. A quorum present and acting.

15. *Association Mailing List:*

Doctor Alesen requested that the Association mailing list be made available to the Investors League, Inc., to aid that organization in its campaign against governmental encroachment on private enterprise in business or professional life. It was regularly moved, seconded and voted that the mailing list be made available to this organization and that public relations counsel be asked to give possible assistance in this move.

16. *Legal Department:*

Mr. Hassard reviewed a malpractice case in Lodi, in which new judicial interpretations of the law had emerged. He stated that his office, acting on Executive Committee authorization by telephone, had filed a brief as amicus curiae. The Council approved this step and authorized the moderate printing and filing costs involved.

Mr. Hassard also reviewed the opinion rendered by the Attorney General of California holding that a hospital may not engage in the practice of medicine through the employment of physicians on salary. A New York attorney for the American Hospital Association has rendered an opinion that *non-profit hospitals* may engage physicians on salary but the attorney for the Association of California Hospitals has advised his client that the Attorney General's opinion is sound and must be followed. A conference is scheduled for November 8, 1948, to discuss this matter and Mr. Hassard has been invited to attend.

17. *Public Policy and Legislation:*

Dr. Dwight H. Murray, chairman of the Committee on Public Policy and Legislation, distributed copies of a draft of a proposed bill to establish a "Practical Nurses Act" prepared by the California State Nurses Association. After discussion it was regularly moved, seconded and voted to appoint a committee to meet with nurse association representatives to discuss this proposal. The Chairman named Doctor Murray, Doctor MacLean and Mr. Hassard to this committee.

Doctor Murray also discussed a physical therapy bill which is expected to be introduced in the next Legislature, similar to previous bills of this nature which have consistently been defeated. Representatives of recognized physical therapy schools have requested Mr. Hassard to draft a suitable bill for their presentation in the Legislature, which he had agreed to do provided (1) the Council approve and (2) he would be solely entrusted with such draft and its progress in the Legislature. On motion duly made and seconded, Mr. Hassard was authorized to proceed on this basis.

Mr. Read gave a brief report on the California election campaign and Mr. Boyle reported on the national legislative outlook.

A resolution adopted by the Council of the San Diego County Medical Society, decrying the proposed establishment of Social Security laws to cover self-employed individuals and urging a stand against such legislation, was read and it was regularly moved, seconded and voted that the substance of the resolution be approved and the San Diego Council commended for its activity and interest in this matter.

Letters from two members, urging support for Marjorie Shearon, Ph.D., were read and it was regularly moved, seconded and voted to continue the Association's support of her service.

18. *Diabetes Survey:*

A letter from the Alameda County Medical Association, reporting on a proposed county-wide survey for diabetes, was read and it was regularly moved, seconded and voted to disapprove this project.

A second proposed diabetes survey, sponsored by the American Diabetes Society, was approved, with the provision that the survey be conducted through the appropriate county medical societies.

19. *Committee Report on Membership Qualifications*

A report by a special committee under the chairmanship of Dr. John W. Cline on a resolution introduced by Dr. Wilbur Bailey at the 354th Council meeting, was read and, with minor amendments, approved.

20. *California Ambulance Association:*

Doctor Hoffman reported on meetings with representatives of the California Ambulance Association, which is seeking medical advice in setting up a code of ambulance standards, and urged that cooperation of the Association be extended. Doctor Hoffman has been asked to sit as a non-voting member of the organization's executive board and to address its meeting in Fresno on November 21, 1948. The Council approved these requests.

21. *Crippled Children's Program:*

Attention was called to Resolution No. 23 adopted by the 1948 House of Delegates relative to an investigation into the authority of officials in administering the Crippled Children's Act and it was regularly moved, seconded and voted that a committee for this purpose be appointed. The Chairman appointed Drs. John C. Sharp and Lloyd Hardgrave.

22. *Sister Kenny Foundation:*

A request for Association cooperation in the administration of the program of the Sister Kenny Foundation was read. It was pointed out that the San Francisco County Medical Society has been studying a similar request and it was agreed to await word from that study before further Council consideration is given.

23. *Employees' Retirement Program:*

Doctor Charnock reported that a life insurance-retirement annuity policy has been issued to the Association on the life of John Hunton. The committee has not yet met to consider recommendations for extending this program to other employees who might become eligible.

24. *American Public Health Association:*

Attention was called to a meeting in Boston, November 8-12, of the Committee to Consider Establishment of a Medical Care Section of the American Public Health Association. It was regularly moved, seconded and voted to appoint a C.M.A. representative to attend this meeting, the Chairman to select the representative. Dr. William P. Lucas, a fellow of the A.P.H.A., was appointed.

25. *General Practitioner of 1948:*

Mr. Hunton reported that only one nomination had been received from county medical societies for nomination by the Association to the A.M.A. for consideration for the General Practitioner award for 1948. It was agreed to ask the Executive Committee to await further nominations and to make a selection for nomination at the latest available time.

26. *A.M.A. Grass Roots Conference:*

On motion duly made and seconded, Dr. Robertson Ward was elected as C.M.A. representative to the "Grass Roots" Conference of the A.M.A.

Veterans' Views on the Home Town Medical Care Program

A recent survey was initiated by California Physicians' Service, at no expense to the government, in order to determine the effectiveness of the Veterans Home Town Care Program. The veterans who have received treatment were asked to judge how successful the California Physicians' Service had been in rendering treatment. Comments were requested bearing on all phases of the program, particularly in contrast to other types of medical care which they, as veterans, have received in the past.

FAVORABLE COMMENTS

1. Free choice of physician provides personal care which is better than any other method	54%
2. Saves time and trouble while permitting self-employment and education	15%
3. Provides relief from congestion in VA hospitals with a minimum of "red tape"	10%
4. Ability to maintain home due to relief from financial burden	7%
5. Specific requests to continue program	6%
	92%

UNFAVORABLE COMMENTS

1. Delay in treatment 2. Delay in payment of bills 3. Red tape	8%

The unfavorable replies represent cases which require either a change in the law, further coordination within our own offices, or improved liaison with the Veterans Administration.

It is to be noted that the written replies received conform to the verbally expressed opinions of the hundreds of veterans who have called personally at our offices.

The final conclusion must be that this plan has filled a tremendous gap in completing the desire of the government to give the best and most adequate care to our disabled veterans, and that the plan, its administration, and its effectiveness, while not perfect, is preponderantly the best yet developed for ambulatory cases.

The success of the program has been made possible due to the excellent cooperation of the physicians, the veterans, the California Physicians' Service and the officials of the Veterans Administration in California whose daily assistance has been most important.

27. *Insurance Payments to Chiropractors:*

A resolution from the Sacramento Society for Medical Improvement was read, objecting to plans of some insurance companies to provide payment for chiropractic services under accident and health insurance policies. It was regularly moved, seconded and voted to advise the Society that the Council agreed with the resolution and would take the matter up with the insurance companies.

28. *U. S. Public Health Service Tuberculosis Meeting:*

A request from the U. S. Public Health Service to use the Association's mailing list in arranging a San Francisco Bay Area meeting on tuberculosis problems was discussed and approved.

29. *Time and Place of Next Meeting:*

It was agreed that the next meeting of the Council should be held in San Francisco on December 18 and 19, 1948.

30. *California Farm Bureau Federation—Brucellosis Proposals:*

A report from Dr. Paul Michael of Oakland on a meeting of the California Farm Bureau Federation in connection with proposals for the control of brucellosis was read and approved. It was voted to commend Doctor Michael for his efforts in this matter and to suggest his continued interest.

Adjournment.

In Memoriam

Ballard, Samuel Edward. Died in Long Beach, September 20, 1948, aged 74. Graduate of the Baltimore Medical College, Maryland, 1899. Licensed in California in 1916. Doctor Ballard was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

Brown, Henry Alexander. Died in Los Altos, September 19, 1948, aged 77, after an extended illness. Graduate of the Medico-Chirurgical College of Philadelphia, 1900. Licensed in California in 1917. Doctor Brown was a retired member of the Alameda County Medical Association, and the California Medical Association.

✤

Cruice, Leman Dow. Died in Alhambra, September 27, 1948, aged 60, of a heart attack. Graduate of the Jefferson Medical College of Philadelphia, Pennsylvania, 1913. Licensed in California in 1931. Doctor Cruice was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

Engstrom, Walfred A. Died in South Gate, October 23, 1948, aged 40, when he was struck by an automobile. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1944. Licensed in California in 1944. Doctor Engstrom was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

Farrage, James. Died in Corona, October 5, 1948, aged 48, of a heart attack. Graduate of the University of Southern California School of Medicine, Los Angeles, 1934. Licensed in California in 1934. Doctor Farrage was a member of the Riverside County Medical Society, the California Medical Association, and the American Medical Association.

✤

Hallock, Phillip. Died in Los Angeles, June 29, 1948, aged 46. Graduate of the University of Minnesota Medical School, Minneapolis, 1929. Licensed in California in 1945. Doctor Hallock was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

Horner, Warren Douglas. Died in San Francisco, October 22, 1948, aged 58, following an extended illness. Graduate of the University of California Medical School, Berkeley-San Francisco, 1916. Licensed in California in 1916. Doctor Horner was a member of the San Francisco County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

James, Voyle Musser. Died in North Hollywood, October 17, 1948, aged 49, of a heart attack. Graduate of the New York University College of Medicine, New York, 1924. Licensed in California in 1927. Doctor James was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

Jones, Llewelyn L. Died in Glendale, October 17, 1948, aged 77, when he was struck by an automobile. Graduate of the University of Nashville Medical Department, Tennessee, 1899. Licensed in California in 1921. Doctor Jones was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

Jones, Robert Melvin, Jr. Died in Bakersfield, October 17, 1948, aged 66, after a long illness. Graduate of Vanderbilt University School of Medicine, Nashville, Tennessee, 1913. Licensed in California in 1913. Doctor Jones was a member of the Kern County Medical Society, the California Medical Association, and the American Medical Association.

✤

Laist, Otto. Died in San Francisco, October 13, 1948, aged 77. Graduate of the College of Physicians and Surgeons of San Francisco, 1900. Licensed in California in 1900. Doctor Laist was a retired member of the San Francisco County Medical Society, and the California Medical Association.

✤

Reed, Edward North. Died in Sawtelle, October 19, 1948, aged 71. Graduate of Rush Medical College, Illinois, 1904. Licensed in California in 1914. Doctor Reed was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

✤

Sherman, Benjamin Harry. Died in Los Angeles, October 18, 1948, aged 69. Graduate of Northwestern University Medical School, Chicago, Illinois, 1904. Licensed in California in 1915. Doctor Sherman was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

Sperry, John Augustus. Died in Burlingame, September 29, 1948, aged 66, of a heart attack. Graduate of Tulane University of Louisiana School of Medicine, New Orleans, 1905. Licensed in California in 1917. Doctor Sperry was a member of the San Francisco County Medical Society, the California Medical Association, and the American Medical Association.

✤

Williams, Forrest Earl. Died on a train west of Evansville, Wyoming, aged 53, of coronary thrombosis. Graduate of the Northwestern University Medical School, Chicago, Illinois, 1924. Licensed in California 1939. Doctor Williams was a member of the Monterey County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Appointment of Dr. Myron W. Husband as district health officer for the Glendale district of the Los Angeles County Health Department has been announced by Dr. Roy O. Gilbert, county health officer. The appointment fills a vacancy created by the resignation of Dr. Francis Hillman. Dr. Hiram Gallagher, member of the staff who administered the office until Dr. Husband was appointed, will remain as assistant.

* * *

Dr. Paul Starr, member of the faculty of the graduate division of the University of Southern California School of Medicine, has been appointed professor of medicine and acting chairman of the department of medicine, according to announcement from the office of Dr. Burrel O. Raulston, dean of the medical school.

* * *

The first annual mid-winter radiological conference sponsored by the Los Angeles Radiological Society will be held in the Biltmore Hotel, Los Angeles, February 26 and 27, 1949. Courses will be given by prominent Pacific Coast radiologists, and on Saturday evening, February 26, Dr. Frederick Templeton of Seattle will speak on "The Differential Diagnosis of Benign and Malignant Gastric Lesions." Reservations can be made by writing Dr. Donald Laing, 65 N. Madison Avenue, Pasadena 1, California. The fee for the two-day session is $15.

MARIN

A pledge to cooperate with the California Medical Association blood bank program by transporting blood or plasma by plane if necessary in emergencies, such as might arise in connection with disaster, has been given by the Marin County sheriff's air patrol. Glenn Wentz, captain of the air patrol, said that this assistance had been asked in a letter from Dr. John R. Upton, chairman of the California Medical Association Blood Bank Commission which is endeavoring to set up a system for making adequate supplies of blood available for transfusions in all communities in the state.

SAN BERNARDINO-RIVERSIDE

Dr. C. T. Halburg of Redlands was elected president of the San Bernardino-Riverside counties chapter of the American Academy of General Practice at the final organizational meeting of the chapter. Dr. Henry Barron of Riverside was elected vice-president and Dr. Norman E. Marsh, San Bernardino, secretary-treasurer.

SAN DIEGO

A new psychology commission of five members has been appointed for the City of San Diego for the purpose of wiping out the menace of unqualified "psychologists" treating mental disorders. The commission, formation of which was ordered by the city council, will process all licenses of practicing psychologists. Psychologists now practicing and those wishing to enter practice will be required to make formal application for a license.

The members of the new commission are: Dr. Ivan McCollom, head of the psychology department at San Diego State College; Dr. Melvin W. Barnes, director of the University of California Extension Division for the San Diego Area; Dr. Jessie Marcia Ostrander, a clinical psychologist in private practice; Dr. Fay Perry, director of guidance at San Diego State College, and Dr. Thomas Law Coyle, minister of the First Presbyterian Church. Dr. McCollum, Dr. Barnes and Dr. Ostrander are members of the American Psychological Association. The ordinance establishing the commission requires that three of the five members be members of that association.

SAN FRANCISCO

An essay contest with two prizes, one of $150 and the other $100, has been announced by the San Francisco Surgical Society. It is open to physicians in the field of general surgery, residing within a 50-mile radius of San Francisco, who are in the period of graduate training and not more than six years removed from graduation from medical school. Full rules of the contest may be obtained from Dr. Leon Goldman, secretary of the society, University of California Hospital, San Francisco 22.

* * *

Dr. Monroe Jerome Hirsch has been appointed acting assistant professor of physiology at Stanford School of Medicine. He was formerly assistant professor of physiology at Ohio State University and before that a research associate at Stanford.

* * *

A hearing center to which persons with auditory impairment may be referred by physicians for extensive hearing tests and fitting of hearing aids has been established by the San Francisco Hearing Society with the guidance of a committee of otologists working under the San Francisco County Medical Society. Anyone with auditory impairment may avail himself of the services of the center, which is expected to be self-supporting from the fees charged private patients. Fees are on an established schedule but take into consideration the ability of the patient to pay. A recent otologic examination is required, and those not referred to the center by a physician will be given a list of qualified doctors, so that they may impartially select one for the required preliminary examination.

The center is equipped to administer complete pure tone and speech audiometric tests in a sound-treated room. Arrangements have been made with several local dealers of A.M.A.-approved hearing aids to obtain their latest models for demonstration purposes. It is contemplated that in the near future classes and individual instruction in auditory training, lip reading and speech will be available at the center. Eventually, psychological counseling and vocational guidance will be included.

SAN JOAQUIN

Dr. John O. Eccleston recently was appointed city physician of Stockton and director of the Emergency Hospital to take the place of Dr. H. S. Chapman, who resigned several months ago after 28 years' service.

SAN MATEO

Dr. H. L. Wynns has been appointed to the new post of superintendent of field services of the San Mateo County department of health by the county health and welfare advisory board. The new position supplants that of chief of communicable diseases which has been discontinued. Dr. Wynns formerly was assistant district health officer in San Joaquin County, where he served with Dr. Harold D. Chope who is now San Mateo County health director.

SANTA CLARA

The Santa Clara County Mental Health Service, which will be available to adults for advice and consultation on personal matters relative to mental health, has been established with funds allotted by the California Department of Public Health and soon will be in operation. President of the service is Dr. Dwight M. Bissell, who is also president of the Mental Hygiene Society of Santa Clara County, the organization which has been working for establishment of the service. Dr. Rush Faville of Palo Alto will be chief of service.

Directors of the organization said Santa Clara County is one of the few in California having a mental health service of this kind for adults, although recently in San Mateo County a child guidance clinic was established with Dr. Paul Holmer as director.

SOLANO

Establishment of a new county hospital at Vallejo was advocated by a number of Vallejo physicians attending a recent joint meeting of the Solano County Medical Society and the local unit of the Tuberculosis Association which had been called to discuss plans for a hospital for tuberculous patients and expansion of existing county hospital facilities. Pointing out that hospital facilities in Vallejo are inadequate, the Vallejo speakers urged that the county erect a new structure in the area's greatest center of population. It was suggested that the present hospital at Fairfield might then be used as a home for aged indigents.

TULARE

Dr. E. G. Johnson has resigned as assistant director of the Tulare County Hospital to enter private practice but will continue to make visits to the hospital when necessary until the board of supervisors is able to obtain a physician to fill the vacated post.

GENERAL

Of 100 full-time positions open to physicians in tuberculosis hospitals of the Veterans Administration, six are in California, Arizona and Nevada, according to an announcement by the government agency. Salary scale for the posts now open ranges from $4,479 to $10,305. Applicants are asked to address inquiries to Veterans Administration Branch Office 12, 180 New Montgomery St., San Francisco 5, or to Chief Medical Director, Veterans Administration, Washington 25, D. C.

Dr. Donald G. Tollefson, associate clinical professor of obstetrics and gynecology, University of Southern California Medical School, was elected first vice-president of the American College of Surgeons at the annual meeting in Los Angeles, October 21. Dr. Gilbert J. Thomas of Beverly Hills was reelected to the board of regents for a term expiring in 1951. Elected to the board of governors were Dr. H. Glenn Bell and Dr. Emile Holman, both of San Francisco; Dr. Clarence J. Berne and Dr. E. Eric Larson of Los Angeles, and Dr. Clarence E. Rees, San Diego.

* * *

The Phi Delta Epsilon Northern Fraternity, of which some 600 physicians in California are members, will hold its national convention in San Francisco, December 26, at the Fairmont Hotel.

* * *

Dr. William F. Quinn of Los Angeles was elected president of the California State Board of Medical Examiners at a recent meeting, succeeding Dr. Richard O. Bullis, also of Los Angeles. Dr. Clayton D. Mote of San Francisco was elected vice-president of the board, and Dr. Frederick N. Scatena, Sacramento, was reelected secretary-treasurer. Dr. Dan Sooy, formerly of San Francisco and now of Laguna Beach, was appointed to the Board by Governor Warren.

* * *

Announcing its annual cash award contest for 1949, the National Gastroenterological Association says that $100 and a certificate of merit will be given for the best unpublished contribution on gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy. Contestants residing in the United States must be members of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The award for the winning manuscript is to be made at the annual convention banquet of the Association in October of 1949. The Association reserves the exclusive right of publishing the winning contribution, as well as those for which certificates of merit are given, in its official publication, *The Review Of Gastroenterology*. Entries should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies accompanied by an entry letter, and must be received not later than April 1, 1949. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

* * *

Available free from local health officers throughout the state, a unique "Manual for the Control of Communicable Diseases in California" has just been issued by the State Department of Public Health. The booklet lists the communicable diseases in alphabetical order, and describes their significant aspects. Each section groups together the relevant California laws and regulations, information about laboratory diagnosis and the tests available from the State Division of Laboratories, recommended immunization procedures, the present status of specific therapy, and data on the role of the public health nurse. It is planned to revise the manual and correct any errors in approximately one year. To this end the State Health Department invites expressions of criticism and advice.

INFORMATION

Extra Pay, Choice in Assignment Offered by Army to Physicians Accepting Active Reserve Duty

Physicians who volunteer now for active duty in the Army Medical Corps Reserve will be given opportunity to select, within limitations, the place they wish to serve and the type of duty they desire, according to a spokesman for the Sixth Army Reserve.

These and other inducements are being offered to attract volunteers and thus avoid the need for the government to devise other means of procurement.

Increased pay to offset medical education expenses, initial appointment in advanced grades for those who qualify, a liberalized system of promotions, arrangements for internships and residencies, a minimum of administrative "paper" work, and retirement benefits for Reserve officers on active duty equal to those of regular career officers for the proportionate time served, plus some additional credits for time on inactive reserve status—these are among the new inducements offered (see chart, page 482).

Thirty physicians are needed between now and January 1, 1949, to fill Sixth Army requirements for California alone. An additional 60 must be recruited prior to June 1, 1949, and an undetermined number thereafter, according to need. Nationally, the Army's quota for 1949 is 4,000 physicians.

Volunteers may sign up for one, two or three year periods. During the first year of any volunteer service the physician will, where at all possible, be assigned to a post close to his home. The two and three year periods offer the opportunity to request foreign service in the theater of the physician's choice.

A communication from Sixth Army Headquarters in San Francisco details some of the problems:

"Enlargement of the Army due to the draft, and the completion of the tour of duty of the last of the Army School Training Program physicians and dentists, is causing a critical shortage of physicians and dentists for the armed forces.

"Since the Army is receiving the largest augmentation, its needs in this regard are more acute. To meet this situation at least until the government can find a satisfactory solution, we will need the active support of all members of civilian medicine and dentistry.

"We require, primarily, physicians and dentists for professional work in general hospitals, station hospitals, dispensaries and post dental clinics. It is highly desirable, from our standpoint, to secure these professional men on an officer status, and for a duty period of one year or more if possible.

"To solve this [problem of meeting the quotas] we must secure the active support of the whole broad base of medicine and dentistry in this country. . . . The opportunities for a professional man entering the regular service are better than at any previous time in the Medical Department's history. We have a professional training program second to none. Physicians and dentists on extended active duty, or in the Regular Army, receive $100 a month additional pay as compensation for previous professional training.

"We are utilizing these professional men entirely on professional work, and in the field of medicine or dentistry which they most desire, or, at least, have received training for, in civilian life. This is, of course, professionally desirable, administratively feasible, and also necessary to secure the greatest amount of professional service with the minimum of personnel. It also corrects one of the major criticisms of professional men who served during the war.

"For information on this subject, it is desired that you write the Surgeon, Headquarters, Sixth Army, Presidio of San Francisco, California, or contact the post surgeon at the nearest military installation."

The Relationship of the Practicing Physician to the School Health Program

David Van Der Slice, M.D.*

Every practicing physician plays a part in the school health program whether or not he serves as a school physician. The medical services he gives to children in his private office are an integral and important aspect of the program. No program of health education in the schools can be wholly successful without the private physician's active participation and the approval and support of the local medical society.

The American Medical Association, recognizing the need for a closer relationship between the practicing physician and the schools, called a nationwide conference in October, 1947, on the Cooperation of the Physician in the School Health and Physical Education Program. Delegates from nearly every state medical association met with representatives from state departments of health and of education to explore ways in which the physician in private practice can best serve in the school health program. The conference unanimously recommended that "every local medical society set up a school health committee" to act in an advisory capacity to the schools with regard to the health program.† This was declared to be a necessary first

*School health consultant, State Department of Public Health.

†An alternate plan is for the public health committee of the Society to assume this function.

ESTIMATE OF EARNINGS—U. S. ARMY MEDICAL OFFICER WITH TWO DEPENDENTS

(Estimate of Earnings Based on Entrance Into Service at Lieutenant Grade)

Grade	Automatic Promotion Next Higher Grade (1)	Base Pay (2)	Medical Equalization Pay (3)	Allowance (4)	Retirement Benefits for Age (5)	Retirement Disability (6)	Death Gratuity (7)	Tax Differential (8)	Health Insurance (9)	Total Annual (10) (11)
LIEUTENANT	After four years of service	$2,400.00 No prior service	$1,200.00	$1,411.00	$1,050.00	$ 45.90	$13.40	$515.29	$102.00	**$ 6,737.59**
CAPTAIN	After eleven years' service	2,898.00 3 years' service	1,200.00	1,591.00	1,050.00	59.05	16.95	576.02	102.00	**7,493.04**
MAJOR	After eighteen years' service	3,960.00 12 years' service	1,200.00	2,026.50	1,050.00	100.24	27.58	748.07	102.00	**9,214.39**
LT. COLONEL	To Colonel by selection only	5,005.00 18 years' service	1,200.00	2,206.50	1,050.00	157.97	42.77	872.27	102.00	**10,636.51**
COLONEL	To General Officers by selection only	6,380.00 27 years' service	1,200.00	1,951.00	1,050.00	232.54	63.82	910.57	102.00	**11,889.93**

1. Unless he is promoted sooner which, under present conditions can be expected, an officer of the Medical Corps is automatically promoted to the next higher grade at the completion of years service in grade as shown.
2. Base pay is computed on average years service for pay purposes in each grade and is subject to a 5 per cent increase for each additional three years' service to a total of thirty years. Service, active or inactive, performed in any branch of the Armed Services at any time is credited for pay purposes.
3. Regular officers and reserve officers accepted for active duty for one year or more, on duty and appointed between 1 September 1947 and 31 August 1952. This payment limited to 30 years or total of $36,000.
4. Includes allowances for rent and subsistence.
5. Based on figures obtained from the Massachusetts Mutual and John Hancock life insurance companies. To purchase outright at age of sixty-four a life annuity comparable to Army retirement requires $60,000. Such an annuity purchased at age thirty requires $35,700 or thirty-four payments of $1,050. This is the figure shown in the table. The difference between $60,000 and $35,700 represents the amount of interest on the annual premiums and deductions made possible by the fact that a certain number of policy holders will die before the age of sixty-four. A policy taken out at an age earlier than thirty would of course have a lower annual premium. Reserve officers receive retirement pay at age sixty proportional to total active duty plus certain credit for inactive duty.
6. Cost of disability policy which pays benefit equal to Army disability retirement benefit. Based on figures from Acacia National Life Insurance Company.
7. Cost of insurance policy which pays at death, amount equal to Army six months, death gratuity. Based on figures from Acacia National Life Insurance Company.
8. Represents the income tax differential between an officer's salary and an equivalent civilian salary. Figures are based on deductions for subsistence, quarters, and the $1,500 special military exemption which is now effective and the continuation of which is expected in pending legislation.
9. The cost of a civilian health insurance policy providing benefits similar to those made available to an Army officer (Group Health Associations, Inc., figures as of 1 December 1946). There is no civilian policy which offers all the benefits available to an Army Medical Officer.
10. This table is not altogether complete because flight pay, parachutists pay, foreign service pay, commissary privileges, uniform and travel allowances, etc., are not included.
11. In addition to death gratuity pay the dependents of an officer who dies while on active duty from a service connected disease or injury is entitled to a pension, which in the case of a wife and two dependent children will be $720 or $1,380 annually, depending on whether death was due to conditions which developed during peace or war time service. A life annuity income paying such sums for a woman thirty years of age would cost $15,000 and $29,000 respectively.

step in achieving the practicing physician's cooperation and participation.

The schools need and welcome assistance from local practicing physicians in planning the school health program and in developing written policies and procedures patterned to fit local needs. The physician can make this contribution by serving on the advisory school health council.

The practicing physician renders one of his most important contributions to the school in his role of medical examiner, whether he sees the children in his private office or at the school. The medical examination gives the physician an opportunity to evaluate the pupil's health status in terms of physical and emotional growth and development, soundness of health practices and attitudes and general fitness to participate in the various school activities. Medical examinations of children performed at the school should demonstrate a high quality of medical service and be a satisfactory educational experience both to the child and his parent. An important objective is to develop an appreciation of and a desire for continued medical advice and guidance by the personal physician.

The chief purpose of medical examinations performed at the school is not to make a detailed diagnosis but rather to screen out any serious health problem which handicaps the child and, where indicated, impress upon the parent the importance of seeking further professional attention. The best place for the child to secure periodic medical examinations is in the office of his own physician who has previous knowledge of his health, has the facilities to make a thorough health appraisal and will give him continued health supervision. Experience has shown that when schools through an educational program and a definite administrative policy actively encourage pupils to obtain periodic medical examinations from their private physician, a majority of them do so.

The exchange of health information between the school and the physician has been demonstrated to be an important factor in safeguarding the health of the individual child. It is important that teachers know the physical limitations of their pupils; the physician, by sharing his knowledge about a pupil's health, can help the teachers to better understand their pupils and frequently enable them to assist in the solution of their health problems. It also permits an adaptation of the school program where this is necessary, for example, a restricted physical activity program for a child with rheumatic heart disease. The teachers must be made thoroughly aware of the necessity for safeguarding all matters of a confidential nature. A medical examination form, approved by the local medical society, would make possible the channeling of this useful information from the doctor's office to the school.

In recent years teachers have been trained to observe and record noticeable deviations from normal health and behavior in their pupils. Students suspected by the teacher—on the basis of her day by day observations—of having a health problem are referred through the medical department to their private physicians for medical examination. Certain of the information and impressions gained through the teacher's daily observations is very helpful to the physician responsible for medical supervision of the child. An exchange of information about pupils' health enables both physician and school to do a better job of health supervision.

Other ways in which the practicing physicians can contribute to the school health program include:

1. Giving medical guidance to the school's physical education program and to aid in developing uniform policies regarding excuses from physical education.
2. Assisting in a program of in-service education for teachers and school health service personnel.
3. Appraising the health content of the school curriculum in terms of factual accuracy and completeness of coverage.

Practicing physicians can make valuable contributions to the health of the community, as well as to the health of children under their private care, by taking an active part in the health program of the schools.

Diabetes Detection Drive

HOWARD F. ROOT, M.D., *Chairman,*
Committee on Diabetes Detection

The finding of the million unknown diabetics in this country poses a direct challenge to the American doctor. It is within his power to accomplish this feat. The existence of a million undiscovered diabetic patients in the United States has been demonstrated through a series of surveys, the most recent one conducted by the United States Public Health Service. The results of these studies now provide a springboard for organized medicine and a golden opportunity for physicians to seize the initiative *on their own* in this significant phase of public health.

The American Diabetes Association has planned a campaign to promote the early discovery and prompt treatment of the million undiscovered cases of diabetes. This campaign is unique in professional service, for according to plan the physician himself will be at the helm. Therefore, the plan cannot be prosecuted, or even started, without the endorsement and support of the entire medical profession through its governing bodies, national, state, county and local medical societies.

The plan proposed by the association is simple, direct, and sure. Through local diabetes associations, related to the American Diabetes Association and with cooperation of local, county and state medical societies over the United States and Canada, it is planned to carry out blood-sugar screening tests by a new five-minute micro-blood sugar method with simultaneous urinalysis for sugar with attention to the time in relation to the preceding meal. The procedure can be carried out apart from a formal labo-

ratory. The equipment is still in the manufacturers' hands but is to be available within two or three months. The only provision will be that the candidate must name a physician or clinic to which the results of the tests will be mailed for interpretation to the patient. *Under no condition* will a report be sent directly to the examinee. The effort is to bring the unknown diabetic patient under his own physician's care. There will be no statistics; no red tape.

Simultaneously, the American Diabetes Association will carry on an intensive educational campaign directed first toward doctors' post-graduate courses. It will be directed toward the layman by radio, newspapers and other publicity channels in addition to the *A.D.A. Forecast,* the Association's bi-monthly magazine which brings to the diabetic patient homespun articles on the disease by eminent authorities in the field. At the same time the association will place in the hands of physicians over the country an authentic "Handbook of Therapy." Containing the most up-to-date information available, the handbook will assist the physician in treating diabetic patients.

The week of December 6-12 was proclaimed as "Diabetes Week." This was the formal beginning, the kick-off, of the association's diabetes detection drive. From this start, the program will continue on a long-term basis.

The association is determined to do its part in finding these million individuals and guiding them to you, their physicians, for treatment. May we count on your support when the matter comes up before your county or local medical society? The success or failure of the diabetes detection drive depends upon you. *You* stand at the helm; this is *your* project.

BOOK REVIEWS

DIAGNOSIS IN GYNAECOLOGY—A Classification of Gynaecological Diseases Based on Aetiology and the Clinical Logic of Diagnosis. By James V. Ricci, A.B., M.D., Clinical Professor of Gynaecology and Obstetrics, New York Medical College. The Blakiston Company, Philadelphia & Toronto, 1948. 259 pp., no illustration.

This small volume resulted from efforts to teach gynecological history-taking and examination to undergraduate medical students at the New York Medical College. It may have some value in that connection, but its value to the practitioner seems doubtful. The author has taken information which is available in all of the standard gynecologic textbooks and rearranged it to suit his own devices. After brief descriptions of pelvic anatomy and embryology, as well as the female sex hormones, there follow many details about the performance of gynecological examinations. Under "special types of examination" there is no mention of the Papanicolaou smear technique. The rest of the volume concerns itself with classifying pelvic disorders on the basis of what the author insists upon spelling "aetiology." Throughout the book the diphthong is used also in the word "gynaecology." The author's concept of the meaning of the word etiology seems at variance with the generally accepted definition. One wonders what is gained, for example, by stating that "diseases of the uterus result from the following aetiologic factors" and then setting forth a list containing every conceivable uterine disorder, all the way from pyometra to bullet wound of the uterus. There is also some mention of pregnant uteri having been pierced by bulls' horns. Certainly this must occur infrequently in New York City. While the reviewer finds no serious errors of fact in this text, it seems fair to say that it contains very little information which will be of value outside the classroom from which it sprang.

* * *

PRACTICAL BACTERIOLOGY, HEMATOLOGY, AND PARASITOLOGY. By E. R. Stitt, M.D., Rear Admiral, Medical Corps, and Surgeon General, U. S. Navy, Retired; Paul W. Clough, M.D., Physician-in-Charge of the Diagnostic Clinic, Johns Hopkins Hospital; and Sara E. Branham, M.D., Senior Bacteriologist, National Institute of Health, and Contributors. Tenth Edition. The Blakiston Company, Philadelphia.

Republished for the first time since 1938, the tenth edition of this book, which was originally published by Rear Admiral E. R. Stitt in 1909 and since that time has been a very popular textbook covering principally the techniques of bacteriology, hematology, and parasitology, has been entirely revised by Stitt, Clough, and Branham and is contributed to by other authors.

Primarily a text on laboratory technique, it covers the various subjects in a complete and acceptable manner. It is particularly outstanding in the fields of bacteriology, serology, and parasitology. The section on diseases of the blood is excellent when viewed in the light of its obvious functions, but should not be confused with a reference text giving an exhaustive coverage of hematology.

Its outline and the manner in which much detail is presented continue to make it one of the most outstanding books in this field. The references to clinical applications, which form an integral part of each topic which is presented, increase its practicability. It must not be considered just a textbook for medical students and technicians. It is designed to fill a much greater function, and strengthened by the section covering the techniques of the examination of various body fluids and organs, it becomes a practical text, not only for those in the profession of medicine who routinely or occasionally perform laboratory procedures, but also for those research workers, clinicians, or teachers who are true medical scientists.

The material is well arranged in such manner that the text is readily usable for specific reference work. The bacteriology, immunology, hematology, and parasitology are very properly conveniently separated from each other with overlapping of material only for purposes of clarity and accuracy.

The book can heartily be recommended as a valuable text for students and as a useful guide and reference book for the practitioner of medicine.

* * *

MEDULLARY NAILING OF KUNTSCHER. By Lorenz Böhler, M.D., Director of the Hospital for Accidents in Vienna; Professor of Surgery at the University of Vienna. First English Edition revised by the author. Translated from the Eleventh German Edition by Hans Tretter, M.D., Surgeon in Charge of the New Jersey Manufacturers Hospital. The Williams & Wilkins Company, Baltimore. 1948. $7.00.

Like many other fracture surgeons Lorenz Böhler has always sought a simple method of internal fixation which could be applied *without opening the fracture site.* In 1940 Küntscher described such a method. This consists in the insertion of a long, hollow, strong steel (V_2A) rod through a small incision at one end of the bone down through the medullary canal across the fracture site deep into the distal fragment. When Böhler saw this procedure it appealed most strongly to him. Here at last was a simple method of securing internal fixation *without opening the fracture.* Thus the important fracture hematoma was preserved, risk of infection was practically nil, early muscle function and joint movement along with weight bearing was possible and finally *callus formation and fracture healing were accelerated.* It was fantastic. He quickly resolved to adopt the method. Anatomical studies were carried out to determine the exact width, length and direction of the medullary canals so that length, width and curve of nail could be accurately figured.

Two hundred sixty-eight cases have been operated upon in the Viennese Hospital for traumatic surgery. This series embraces not only fresh fractures of all the long bones, but includes many old ununited fractures, nonunions, malunions, pseudo-arthroses, bone shortening operations, spontaneous fractures, etc. In addition Böhler has had an opportunity to study the records, x-rays, patients, and end results of over 300 Küntscher nailing operations performed in other hospitals.

This extensive experience permits the author to describe in great detail the instruments and apparatus required, the exact technique for inserting the nail, the kind of case suitable for the method, the postoperative care, and the reasons for possible success or failure.

The method, which at first seemed so simple, has in fact turned out to be so complicated that it quite obviously can be used only by surgeons of great experience with much expensive and complicated apparatus available. For example, a fractured femur requires a specially designed traction frame, 36 special instruments or apparatus which includes two mobile fluoroscopic units, a fluoroscopist, x-ray technician and an anesthetist in addition to the surgeon, his assistants and the regular operating room nurses.

Careful study of over 600 cases has brought to light an "almost unbelievable number" of complications and end results. Death, comparatively frequent infection, faulty position of fragments, faulty position of nail, splitting bone with nail, rotation of fragments, migration of nail into joint, broken nail, and many others have been recorded.

Careful observation has proven that the massive spindle of callus seen in some of the earlier cases was in fact due either to the irritation resulting from corrosion of poor quality steel nails or to persistent slight movement at the fracture site (nail too short or too long). Such massive callus is of poor quality and in these cases actual fragment fusion is very slow. *Actually callus formation and fracture healing are somewhat impeded by the presence of the nail in the medullary canal.* This observation, verified by Maatz at the Kiel Clinic in 300 cases, "constitutes the greatest disappointment that I have experienced as a physician, because I had set the highest hopes upon the callus-stimulating effect of the medullary nail." Furthermore "it is evident that closed medullary nailing is suited chiefly for transverse fractures of the femur in the middle third." In addition, perhaps in the hands of certain expert bone surgeons, the nail can be used in selected cases of nonunion, where the fracture must be exposed to freshen the bone ends or insert grafts (open nailing), in bone shortening operations, and certain pathological fractures.

The book is highly recommended to all surgeons who treat fractures. It tells everything that is known about medullary nailing. The chapter on "callus" is a classic. Böhler's observations on the results of skeletal traction are sound and practical. These alone are worth the price of the book.

* * *

BRITISH SURGICAL PRACTICE VOL. I. Under the General Editorship of Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital, and J. Paterson Ross, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. In Eight Volumes (With Index Volume), Butterworth & Co. (Publishers), Ltd., London, England. The C. V. Mosby Company, St. Louis, Mo., U.S.A., 1947. $15.00.

As one reviews this first volume of an eight-volume system of surgery, he is impressed by the very substantial, high quality paper upon which it is printed and by the consequent excellent appearance of its illustrations.

The subject matter is excellent, also, although one misses a brief historical resumé of the subject and, in certain disorders, a more detailed account of their pathologic physiology. Excellent suggestions as to treatment abound. What it lacks in a coherent, well-integrated account such as one expects from a textbook authored by a single person, it gains in the greater completeness and more authoritative treatment provided by numerous experts in their fields.

One is a little puzzled to find so many unrelated subjects covered in the same volume and to find "peripheral arterial diseases" included in the chapter devoted to the "autonomic nervous system" instead of under "arteries." When all eight volumes lie before one, however, reference to related conditions will undoubtedly be made easily and we trust without confusion, and without unnecessary repetitious accounts of the subject. One awaits the succeeding volumes with real anticipation that reading them will be amply rewarded.

* * *

THE NURSING OF TUBERCULOSIS. By O. V. Buxton, S.R.N., and P. M. Maculloch Mackay, S.R.M.N., with a Foreword by Richard R. Trail, M.C., M.D., Illustrated by Nora Lewis, S.R.N. John Wright & Sons, Ltd., Bristol, Simkin Marshall (1941), Ltd., London, 1947. $2.00.

In the preface of this brief volume the authors mention that it is "written expressly for the nurses and student nurses engaged in the nursing of tuberculous patients." The subject material is well covered. The illustrations are very helpful for the student.

As can be expected there is variation in terminology and spelling which may confuse student nurses. The indications listed for various procedures may also not agree with some of the teachings of American chest specialists. For this reason it may be advisable to recommend this book for graduate nurses interested in diseases of the chest rather than as a standard text for student nurses.

* * *

HANDBOOK OF OPHTHALMOLOGY. By Everett L. Goar, A.B., M.D., F.A.C.S., Professor .of Ophthalmology, Baylor University College of Medicine, Houston, Texas. With 48 Text Illustrations and 7 Color Plates. St. Louis. The C. V. Mosby Company. 1948. $5.50.

This handbook of Ophthalmology is the result of the setting down of his lectures to medical students by the author. In so doing, he has given a brief description of the commoner means of examining the eye, and the commoner eye diseases. He has also very briefly mentioned methods of treating eye diseases without going into details. There are some excellent illustrations in the book which add to its value. It would make a good handbook for someone who wished a superficial knowledge of facts about ophthalmology without ever expecting to treat the eye.

* * *

PRACTICE OF ALLERGY. By Warren T. Vaughan, M.D., Richmond, Virginia. Revised by J. Harvey Black, M.D., Dallas, Texas. Second Edition. The C. V. Mosby Company, St. Louis. 1948. $15.00.

The publication of a Second Edition of Vaughan's Practice of Allergy with revisions by Dr. J. Harvey Black is of importance to the field of Allergy. The first edition of the Practice of Allergy appeared in 1939. Since then many books in this rapidly developing field have appeared but none possess the quality, flavor and distinction which its erudite author gave it. Warren Vaughan's book still remains a historical bridge between our old concepts of the underlying causes of allergic manifestations and our newer interpretations.

In common with all publications in so broad a field by a single author, it has the usual weakness, that no one author can write authoritatively on all phases of the subject. This has been partly overcome by the addition of a chapter on Pollen Surveys in the United States and Adjacent Areas and Field Surveys and Aerobiology by Oren C. Durham, an expert in the field. Dr. J. B. Howell has rewritten the chapter on Fungus Infection with Associated Allergy, a phase of allergy which needs much clarification. The chapter on Vital Capacity by Dr. James Holman is a brief but important addition to our understanding of the pathologic physiology of the respiratory mechanism in bronchial asthma.

Finally it should be stressed that there are few books on Allergic Diseases which present so clearly the original concepts of the late Dr. Vaughan on the Balanced Allergic State or Allergic Equilibrium and Food Groups. The revisionist is to be commended for retaining these in the vivid wording of the First Edition.

Since its first appearance in 1939, the reviewer has found Vaughan's Practice of Allergy an excellent reference book and he feels assured that it will be helpful as a guide, not only to the general practitioner but also to the specialist in Allergic Diseases.

* * *

SURGICAL DISORDERS OF THE CHEST. By J. K. Donaldson, B.S., M.D., Associate Professor of Surgery and in charge of Thoracic Surgery, University of Arkansas School of Medicine, Little Rock, Akansas. Second Edition, pp. 485, Lea and Febiger, Philadelphia, 1947. Price, $8.50.

The main additions to the first edition (1944), are concerned with a more detailed consideration of the advances in traumatic thoracic surgery made in World War II, the treatment of pleurisy, surgical diseases of the esophagus, and operations to correct congenital cardiovascular anomalies.

In his preface, the author states that the volume is primarily designed as a reference book for physicians, surgeons and medical students. He indicates that sufficient technical detail is included to permit the competent general surgeon to treat certain surgical disorders of the chest.

As the most recently published attempt to correlate what is new in surgery of the chest, the book is certainly worthy of serious consideration and careful study. Many medical students and physicians, not specialists, will find it a useful reference text. The inclusion of a chapter on resuscitation and inhalation therapy is a welcome addition to a surgical volume.

On the critical side several features of the book must be discussed. The over-all impression is that the text was written hurriedly. There are far too many references to other sections in the book, particularly following sections. This, combined with frequent parenthesized directions, makes for poor continuity both of text and of thought. Due either to carelessness in writing the original text or too hurried proofreading there are at least 40 examples of misspelled words, unwieldy English and misquoted statistics.

Frontal roentgenograms are not reproduced uniformly in position. Frequently they are inadequate, particularly the bronchograms. This may be due in part, however, to a poorer grade of paper in the second edition.

A few of the more obvious deficiencies in text should be listed. The important role of endoscopic procedures in diagnosis and treatment is nowhere emphasized sufficiently. The inference is made throughout that the thoracic surgeon usually does not perform his own endoscopies, an entirely unwarranted impression.

In general, the illustrations are adequate and many are excellent. Figure 107, page 324, is, however, extremely small and is confusing even to a surgeon with considerable knowledge of hilar anatomy. Unfortunately the colored plates on decortication lack third dimensional detail.

The following lesions should be discussed more completely: carcinoma of the upper esophagus; intrapulmonary cysts and emphysematous blebs; primary carcinoma of the lung and its differentiation from bronchial adenoma; traumatic diaphragmatic hernia.

The surgical therapy of pulmonary tuberculosis is covered rather sketchily. The reviewer disagrees with the expressed opinion that the objective of pneumothorax therapy is complete collapse of the lung (p. 376). The discussion of lobectomy and pneumonectomy in tuberculosis should certainly be enlarged.

Finally, a discussion and description of methods which are now obsolete add nothing to the practicability of a book designed primarily as a working manual for others than thoracic specialists. There are confusing allusions to tourniquet ligation in lobectomy and pneumonectomy. The inference that tourniquet ligation is *ever* indicated in pneumonectomy for carcinoma is challenged.

In conclusion, the rapid improvement of thoracic surgical techniques and the widened indications for operative interference in many thoracic diseases make it advisable that this material be assembled in available form. The author obviously has expended much effort in the preparation of the first and second editions. It is to be hoped that if a third edition is contemplated, more care will be exercised in obtaining smoothness and clarity; that pertinent additions and deletions will result in a more useful compendium.

ARTERIAL HYPERTENSION. By David Ayman, M.D., Instructor in Medicine, Tufts College Medical School. Edited by Henry A. Christian, A.M., M.D., Hersey Professor of the Theory and Practice of Physics, Emeritus, Harvard University. (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as in that work.) Oxford University Press, New York. $2.50.

David Ayman's publications over the past 20 years have made it clear that he is one of the foremost students of arterial hypertension as observed in patients; his earlier papers on the critical evaluation of therapeutic results in this disease are classics. In this short monograph he concisely gives his views as to etiology, pathological physiology and evolution of the disorder. Symptoms, physical and laboratory findings are well discussed, and above all there is a sound discussion of treatment (of psychoneurotic, vaso-spastic and organic symptoms, and of the elevated blood pressure itself). The author gives reasons for his belief in the value of thiocyanates and sympathectomy in lowering pressure levels.

A few minor criticisms may be ventured. The reviewer happens to disagree with Ayman's concept of the relation of hypertrophied myocardial fibers to heart failure, and with his use of the word "hypertrophy" in much of the discussion on x-ray of the heart. Adrenal medullary tumor is not acknowledged to be a cause of hypertension other than of the paroxysmal type.

These rather academic points should not obscure the fact that here is an outstanding work by an eminent authority, a work which every medical student, teacher and physician should read carefully and preferably own.

* * *

PROGRESS IN NEUROLOGY AND PSYCHIATRY—An Annual Review Vol. III. Edited by E. A. Spiegel, M.D., Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine, Philadelphia, Pa. Grune & Stratton, New York, 1948. $10.00.

This review, the third in the annual series, maintains the high standard of quality shown by its predecessors. The fields of neurology and psychiatry are covered thoroughly in the 661 pages of the volume, of which 420 are devoted to neurology. As is natural in such a compendium, the quality of the individual reviews varies widely, from a scholarly critical account of recent work and thought on a subject, as exemplified by Schwab's article on Electroencephalography, to a rather prosaic cataloguing of relatively unrelated papers. In all, however, the work is readable and informative and, after its original perusal, constitutes a handy reference book to the recent literature. It can be recommended to the physician who wishes to keep abreast of current thought in this field.

* * *

PEDIATRICS FOR NURSES. By Arthur G. Watkins, M.D., F.R.C.P., Physician in Children's Diseases, Cardiff Royal Infirmary. Illustrated. The Williams and Wilkins Co., 1948. $3.50.

This book is an excellent reference book for nurses in the United States. It is written by a physician apparently without active collaboration of a nurse, which is contrary to the usual practice in our country. The book also particularly presents problems from the point of view of another country, which is always stimulating and refreshing. There is considerable variation in the types of diseases seen in different countries as well as in the approach to therapy. The book might be read with profit by medical students and resident physicians to acquaint themselves with procedures to be learned from the nursing profession.

CALIFORNIA MEDICINE

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KEY TO ABBREVIATIONS USED IN INDEX

(Or.)—Original Article.
(Ed.)—Editorial.
(MP)—Medical Progress.
(CPC)—Clinical-Pathological Conference.
(CC)—Clinical Conference.
(CMA)—California Medical Association.
(CR)—Case Report.
(I)—Information.
(LE)—Letters to the Editor.
(MJ)—Medical Jurisprudence.

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